UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from ____ to ____
Commission file number: 001-37798

Selecta Biosciences, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**26-1622110**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
65 Grove Street, Watertown, MA	**02472**
(Address of principal executive offices)	(Zip Code)

(617) 923-1400
Registrant's telephone number, including area code

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	SELB	The Nasdaq Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports); and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No o

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☐
Non-accelerated filer ☒	Smaller reporting company ☒
	Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attested to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of common stock held by non-affiliates of the registrant based on the closing price of the registrant's common stock as reported on the Nasdaq Stock Market on June 30, 2021, the last business day of the registrant's most recently completed second quarter, was $366,839,496.

As of March 4, 2022 the registrant had 124,288,850 shares of common stock, par value $0.0001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2022 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission are incorporated by reference into Part III of this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or the Annual Report, contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, the plans and objectives of management for future operations and future results of anticipated products, the impact of the COVID-19 pandemic on our business and operations and our future financial results, and the period over which we estimate our existing cash and cash equivalents will be sufficient to fund our future operating expenses and capital expenditure requirements are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential”, or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of important factors that could cause actual results to differ materially from those in the forward-looking statements, including the factors described under the sections in this Annual Report titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” as well as the following:

- our status as a development-stage company and our expectation to incur losses in the future;
- our future capital needs and our need to raise additional funds;
- our ability to build a pipeline of product candidates and develop and commercialize such pipeline;
- our unproven approach to therapeutic intervention;
- our ability to enroll patients in clinical trials, timely and successfully complete those trials and receive necessary regulatory approvals;
- our ability to access manufacturing facilities and to receive or manufacture sufficient quantities of our product candidates;
- our ability to maintain our existing or future collaborations or licenses;
- the continuing impact of the COVID-19 pandemic on our operations, the continuity of our business, including our preclinical studies and clinical trials, and general economic conditions;
- our ability to protect and enforce our intellectual property rights;
- federal, state, and foreign regulatory requirements, including FDA regulation of our product candidates;
- our ability to obtain and retain key executives and attract and retain qualified personnel;
- developments relating to our competitors and our industry, including the impact of government regulation; and
- our ability to successfully manage our growth.

Moreover, we operate in an evolving environment. New risks and uncertainties may emerge from time to time, and it is not possible for management to predict all risk and uncertainties.

You should read this Annual Report and the documents that we reference in this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company. Our ImmTOR® platform encapsulates rapamycin, also known as sirolimus, an FDA approved immunomodulator, in biodegradable nanoparticles ImmTOR is designed to induce antigen-specific immune tolerance.

By combining ImmTOR with antigens of interest, our precision immune tolerance platform has the potential to restore self-tolerance to auto-antigens in autoimmune diseases, amplify the efficacy of biologics (including gene therapies) and mitigate the formation of anti-drug antibodies, or ADAs, against biologic drugs. ADAs can start developing in the body with the first dose of a biologic therapy and can render subsequent doses ineffective or unsafe, potentially depriving patients of life-saving therapeutic options and limiting the likelihood of success for many otherwise promising novel biologic drugs and technologies.

We continually seek to enhance ImmTOR. In recent preclinical studies we have conducted, we have observed that ImmTOR may have synergistic activity with interleukin-2, or IL-2, molecules that have been engineered to be selective for regulatory T cells, or Tregs. Treg-selective IL-2 mutant molecules, or IL-2 muteins, have been shown to transiently expand all pre-existing Tregs in preclinical studies conducted by others. We have observed in preclinical studies that the combination of ImmTOR, a Treg-selective IL-2 mutein and an antigen elicited an approximately three-fold increase in antigen-specific Tregs beyond ImmTOR alone with evidence of enhanced durability of immune tolerance and the potential for ImmTOR dose sparing. This combination of ImmTOR with a Treg selective IL-2 molecule represents an evolution of the ImmTOR platform, which we call ImmTOR-IL™. We believe this combination has the potential to be a best-in-class therapy in diseases where expansion of total Tregs may prove beneficial.

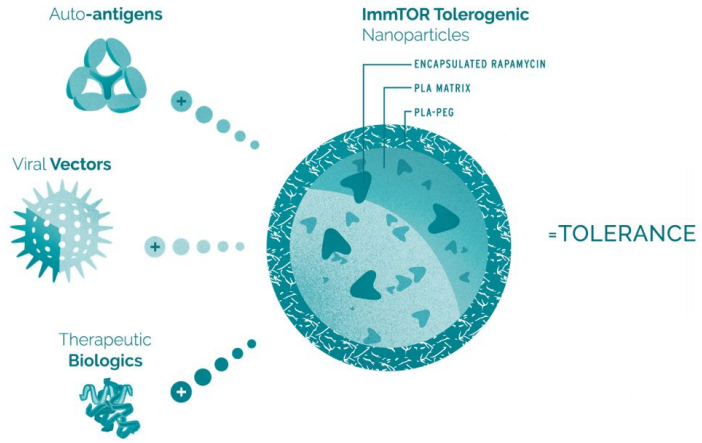
We believe ImmTOR and ImmTOR-IL have the potential to enhance both the efficacy and safety of biologic therapies (including gene therapies), improve product candidates under development, and enable novel therapeutic modalities in autoimmune disease. In clinical trials, ImmTOR has been observed to inhibit the formation of neutralizing antibodies to adeno-associated virus (AAV) capsids, potentially enabling re-dosing of gene therapies. Additionally, based on preclinical data in AAV gene therapies, we believe that ImmTOR has the potential to improve efficacy and safety by increasing transgene expression, reducing hepatic inflammation and inhibiting undesired immune responses to both the AAV capsid and the transgene product that can occur with the first dose of gene therapy. In biologic therapies, clinical activity of ImmTOR in humans has been observed with pegadricase, a highly immunogenic pegylated uricase enzyme being developed for the treatment of patients with chronic refractory gout to conventional therapy. The combination of ImmTOR and pegadricase is currently being evaluated in a Phase 3 clinical trial that we are conducting on behalf of our partner Swedish Orphan Biovitrum AB, or Sobi. We intend to pursue development of therapies for autoimmune diseases where expansion of either all Tregs or antigen-specific Tregs has been shown to, or we believe is, likely to have a beneficial effect. We believe that ImmTOR and ImmTOR-IL have the potential to unlock antigen-specific therapies for autoimmune diseases and that ImmTOR-IL can further improve the efficacy and safety profile of biologic therapies beyond ImmTOR alone.

We have developed a portfolio of wholly owned and partnered candidates across gene therapies, biologic therapies and tolerogenic therapies for autoimmune diseases that leverage our ImmTOR platform. We plan to continue to develop proprietary compounds and pursue collaboration-driven development in certain disease areas, which could include strategic collaborations, out-licensing, and in-licensing transactions.

Our ImmTOR Platform

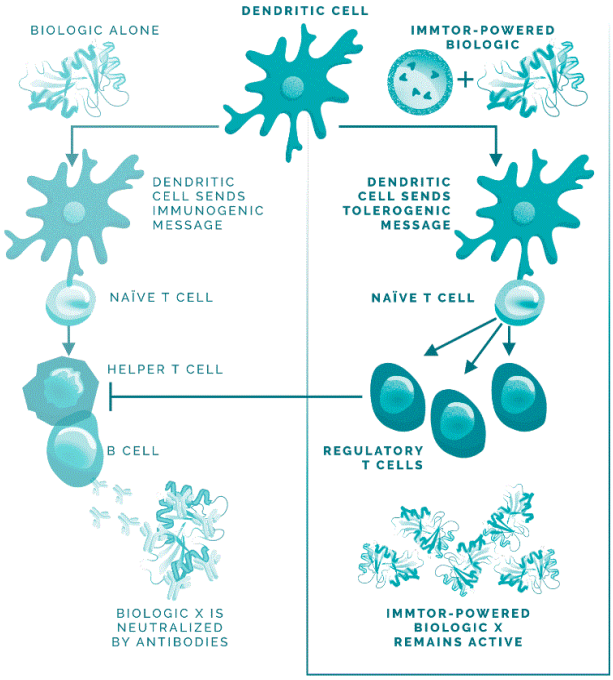
ImmTOR consists of biodegradable nanoparticles encapsulating the immunomodulator rapamycin. Rapamycin is the active ingredient of Rapamune, an immunosuppressant that has been used extensively in humans and is currently FDA-approved as a prophylaxis of organ rejection in kidney transplant patients aged 13 or older. The rapamycin component of ImmTOR is embedded in a matrix of synthetic polymers called poly(D,L-lactide), or PLA, and poly(D,L-lactide)-block-poly(ethylene-glycol), or PLA-PEG. PLA is part of the broader poly(lactic-co-glycolic acid), or PLGA, family of biodegradable polymers that have more than 30 years of commercial use and are formulation components in a number of approved products. Polyethylene glycol, or PEG, has been widely studied in clinical trials and is also a formulation component in many approved biologic products.

Our nanoparticles are designed to remain intact after injection into the body and accumulate predominantly in lymph nodes, the spleen, and the liver, where immune responses are coordinated. The nanoparticles are designed to be processed by specialized immune cells, such as dendritic cells and other antigen-presenting cells, that initiate and regulate immune responses. ImmTOR is intended to induce a tolerogenic phenotype in these antigen-presenting cells, which then process and present co-administered antigens in a manner that results in the induction of antigen-specific regulatory T cells. To mitigate unwanted immune responses by inducing precision immune tolerance in the body, we administer our ImmTOR with the desired antigen, such as an auto-antigen in the case of an autoimmune disease, a viral vector in the case of our gene therapy program, or a therapeutic enzyme, as depicted in the figure below.



In the case of a biologic drug, ImmTOR is designed to be administered in conjunction with such biologic drugs to mitigate the formation of ADAs without requiring the alteration of the drug or its dose regimen. As a result, we believe ImmTOR may provide us with significant opportunities to co-administer ImmTOR with a variety of biologic drugs, including therapeutic enzymes and gene therapies. We believe each pairing of ImmTOR with a biologic drug also offers us the opportunity to pursue distinct proprietary product candidates, which we believe have the potential to be separately patented, approved and marketed. ImmTOR is manufactured in facilities subject to current good manufacturing practice, or cGMP, requirements using well-defined commercial operations, which, we believe, further enhances the scalability of our tolerance programs.

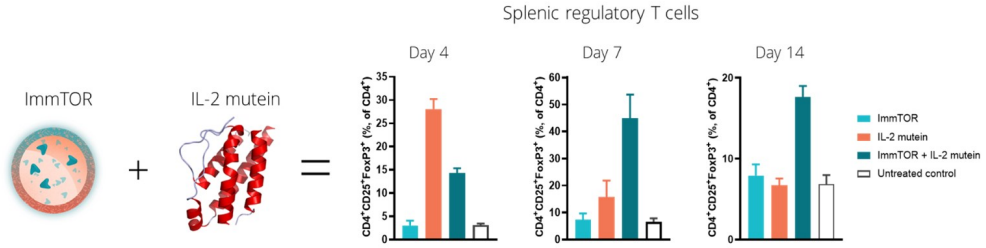
In preclinical studies, we observed that delivering an antigen together with ImmTOR provided the appropriate signals in vivo to induce regulatory T cells, which, in turn, inhibited effector immune responses, such as the formation of ADAs. In additional preclinical studies, we observed that ImmTOR labeled with a fluorescent dye selectively accumulated in the spleen and the liver following intravenous dosing, where it was processed by antigen-presenting cells, such as dendritic cells. The figure below depicts a model of how we believe ImmTOR would be taken up by a dendritic cell in the spleen. We believe that both the biologic drug and ImmTOR are taken up and processed by dendritic cells and other antigen presenting cells in a manner that may result in the activation of antigen-specific regulatory T cells, which can potentially block the activation of helper T cells, thus mitigating the formation of ADAs.



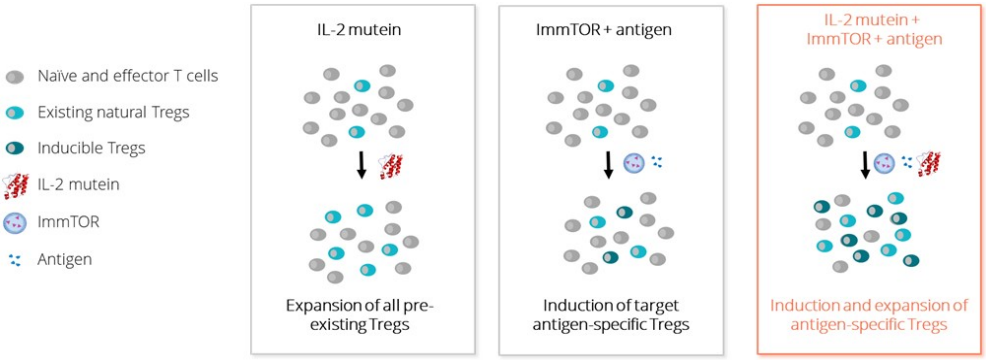
ImmTOR-IL

We look for ways to enhance our ImmTOR platform. Recent preclinical data generated by our scientific teams suggest that ImmTOR may have profound synergistic activity with engineered IL-2 molecules that are selective for Tregs. The IL-2 pathway influences critical aspects of both immune stimulation and immune regulation. Tregs express a high affinity form of the IL-2 receptor. Low doses of IL-2 have been shown by others to selectively activate Tregs resulting in expansion of pre-existing Tregs. Clinical trials of low dose IL-2 have generated evidence of efficacy in autoimmune diseases, such as systemic lupus erythematosus. Other investigators have shown that IL-2 can be engineered to selectively bind to the high affinity IL-2 receptor and expand pre-existing Tregs.

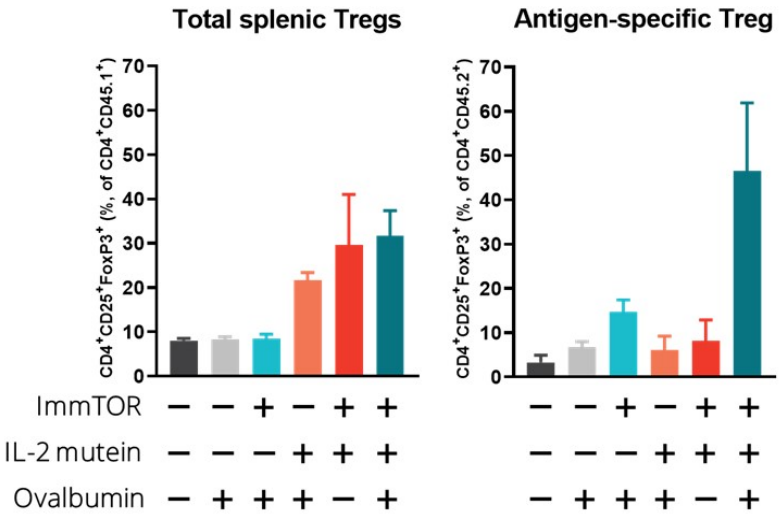
In our preclinical studies, we observed that ImmTOR combined with a Treg-selective IL-2 mutant protein, or IL-2 mutein, exhibited substantial synergistic activity in increasing the percentage and durability of total Treg expansion in the spleen. We believe that this combination has the potential to be a best-in-class therapy in diseases where expansion of total Treg may prove beneficial. The tables below show the synergistic expansion of total Treg we observed with treatment with ImmTOR and a Treg-selective IL-2 mutein. In the study, seven C57BL/6 mice per group were untreated, treated with ImmTOR alone, treated with IL-2 mutein alone or treated with a combination of ImmTOR and IL-2 mutein. Expansion of CD4+, CD25+ and FoxP3+ T regulatory cells in the spleen was assessed at four, seven and 14 days after treatment.



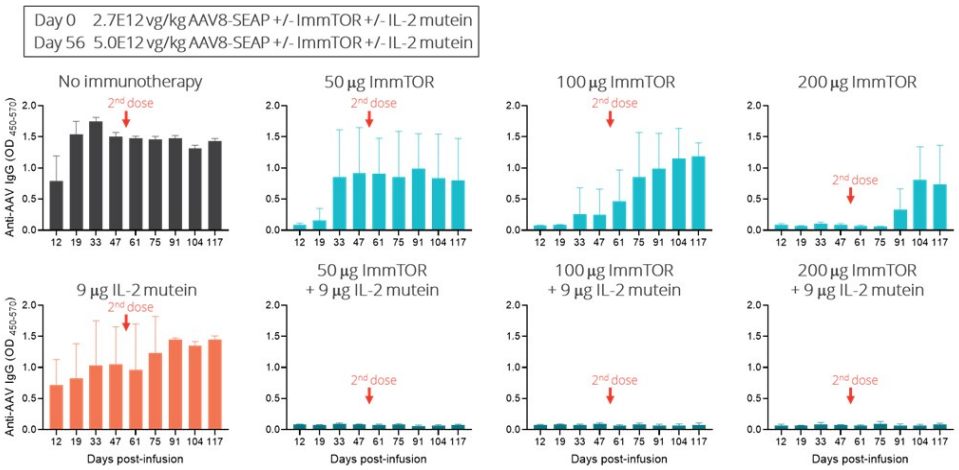
We believe that the power of ImmTOR is the ability to induce antigen-specific Treg to co-administered antigens. The ability to induce antigen-specific Treg may be beneficial in autoimmune diseases where the auto-antigens are well characterized. We believe the combination of a Treg-selective IL-2 with ImmTOR and an antigen has the potential to induce and/or expand antigen specific Treg. The image below illustrates the possibility that the combination of a Treg-selective IL-2 with ImmTOR plus an antigen could give rise to the induction and/or expansion of an antigen-specific Treg.



In a preclinical study, we evaluated the potential of a Treg-selective IL-2 to further expand antigen-specific Treg when combined with ImmTOR and an antigen. In this preclinical study, transgenic T cells expressing a T cell receptor specific for the antigen ovalbumin were adoptively transferred into wildtype mice. The next day, the mice were treated, left untreated or treated with ovalbumin or various combinations of ovalbumin with ImmTOR and/or IL-2 mutein. When total Treg were evaluated, we observed no increase an expansion of total Treg by IL-2 mutein + ovalbumin with a further increase in animals treated with ovalbumin + IL-2 mutein + ImmTOR. As we had expected, ImmTOR + ovalbumin alone did not increase total Treg. However, when ovalbumin-specific Treg were evaluated, we observed a significant increase in antigen-specific Treg in animals treated with the combination of ovalbumin + ImmTOR + IL-2 mutein. Animals treated with only ImmTOR + ovalbumin also were observed to have an increase in ovalbumin-specific Tregs but at levels that were approximately three-fold lower than those in the former group. The following graphs show expansion of antigen-specific Treg in mice treated with ImmTOR plus IL-2 mutein plus ovalbumin antigen.

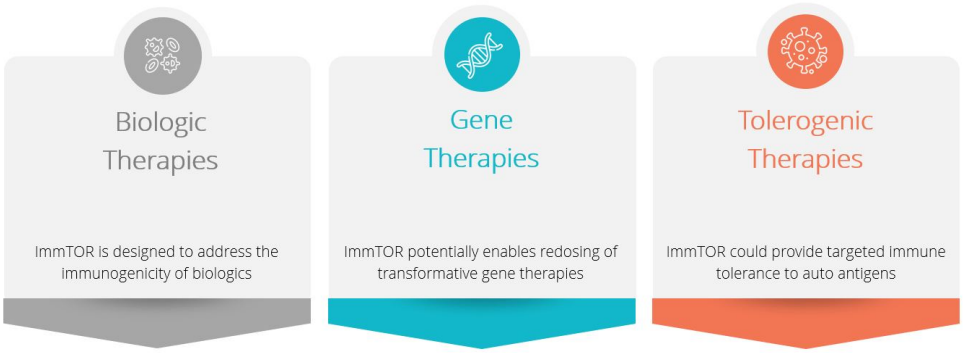


Immune homeostasis is a dynamic process balancing immune stimulatory and immune tolerizing signals. This balance is thought to be mediated in part by the ratio of antigen-specific Treg to antigen-specific effector T cells. The expansion of antigen-specific Tregs has the potential to better withstand potent immune stimulatory signals and provide better durability of immune tolerance. In a preclinical study, we evaluated the ability of ImmTOR and IL-2 mutein to mitigate the immunogenicity to a co-administered AAV vector. Mice were injected with a dose of 2.7E12 vg/kg AAV8 on Day 0 and 5.0E12 vg/kg on Day 56 with or without IL-2 mutein and/or ImmTOR on the same days. Mice treated with AAV alone showed a robust antibody response to the AAV capsid, as we had expected. Co-treatment with IL-2 mutein on Days 0 and 56 showed a modest attenuation of the antibody response. Co-treatment with ImmTOR on Days 0 and 56 showed a dose-responsive effect on the antibody response, with a therapeutic dose of 200 µg ImmTOR providing inhibition of antibodies against AAV through at least Day 75, or 19 days after the second dose. At Day 91, some animals showed breakthrough of the antibody response. ImmTOR doses of 50 and 100 µg alone were sub-optimal. However, when ImmTOR was combined with IL-2 mutein, we observed inhibition of antibody formation through Day 117, 61 days after the second dose and the last time point measured. Importantly full inhibition of anti-AAV immunoglobulin G, or IgG, antibodies was observed even when IL-2 mutein was combined with 50 and 100 µg doses of ImmTOR. We believe these results suggest that the addition of a Treg-selective IL-2 to ImmTOR has the potential to increase the durability of tolerance allow for dose-sparing of ImmTOR and thus, potentially enabling chronic dosing of ImmTOR-IL in the treatment of autoimmune disease. The following graphs illustrate the combination of ImmTOR and IL-2 mutein mitigated the formation of anti-AAV antibodies.



Product Candidates

Our ImmTOR platform has a broad range of potential applications. Our product development strategy is built on the following three distinct pillars.



Biologic therapies. Biologic therapies are a class of biologic drugs frequently used to treat rare diseases. Through our analysis of biologic drugs, including in our preclinical studies, we have observed that enzymes foreign to the human body, such as enzymes derived from microbes or replacement enzymes in the case of patients that are deficient in the specific enzyme, are especially prone to causing undesired immune responses. Our partnered product candidate, SEL-212, which is currently in Phase 3 clinical development, consists of ImmTOR co-administered with pegadricase, a pegylated uricase enzyme of fungal origin. This is an example of an immunogenic enzyme that we are combining with ImmTOR with the intention of improving the enzyme's efficacy and safety. We believe that ImmTOR has the potential to enable and expand the use of enzymes derived from microbial sources, such as bacterial immunoglobulin A, or IgA, protease for the treatment of IgA nephropathy and bacterial IgG protease, or Xork, for the treatment of IgG-mediated autoimmune disease flares.

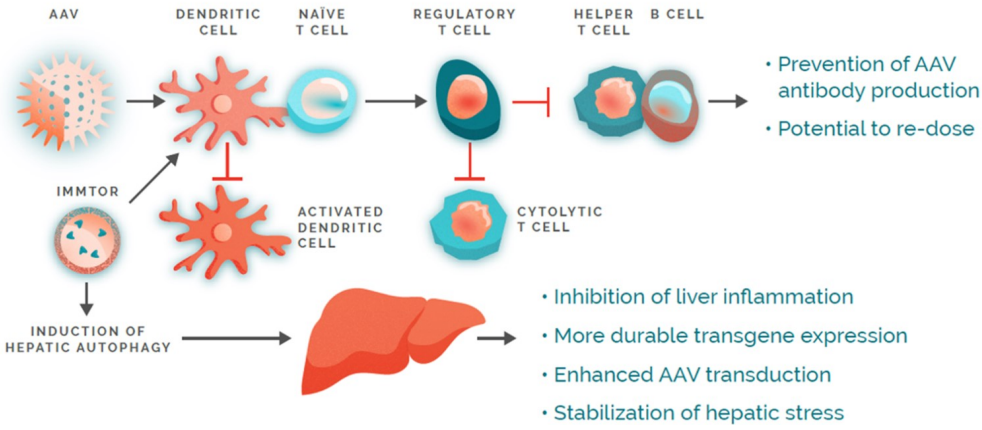
Additionally, we believe advances in protein engineering may lead to innovative therapeutic enzymes with improved pharmaceutical properties or entirely novel specificity and/or activity, but which may be recognized as foreign by the immune system. We are partnering with Ginkgo Bioworks, or Ginkgo, to design novel enzymes and proteins with transformative therapeutic potential which can be paired with ImmTOR to advance treatments for orphan and rare diseases. We intend to seek, if appropriate, licenses to other enzymes to evaluate in combination with ImmTOR.

Gene therapies. We believe gene therapies have the potential to address key unmet medical needs for many rare genetic diseases, but undesired immune responses to the viral vectors used for gene replacement, augmentation and editing may be restricting their broader use. AAV immunogenicity and AAV toxicity represent two major challenges for the gene therapy field; in many cases these two issues are inextricably linked. Immunogenicity of AAV vectors is thought to cause or exacerbate many of the adverse events associated with AAV gene therapy. Induction of acute inflammation and capsid-specific CD8 T cells by AAV gene therapy is thought to contribute to observations of hepatotoxicity, which has been associated with loss of transgene expression. The formation of neutralizing antibodies against AAV after initial treatment with AAV mediated gene therapies effectively prevents the possibility of re-dosing in patients who may benefit from additional doses due to either the failure to achieve therapeutic benefit or loss of transgene expression over time.

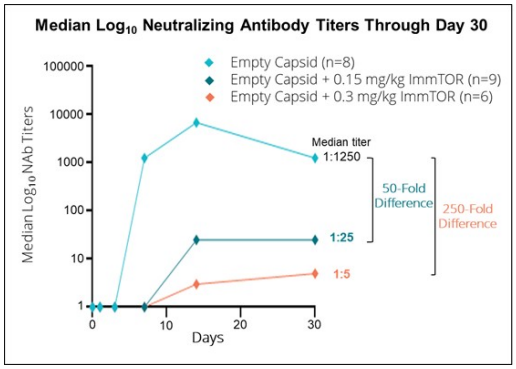
We have observed that ImmTOR, when used in combination with AAV gene therapy vectors, inhibited the immune response to the viral vector and enabled successful re-dosing in both mice and non-human primates. Currently, the ability to re-administer systemic AAV gene therapy is limited by the development of neutralizing antibodies. The ability to safely re-dose AAV may help achieve therapeutic benefit in patients who are under-dosed; it may also help restore transgene expression in patients, particularly pediatric patients, who may lose expression over time as they grow. In a study conducted in non-human primates, or NHP, we observed that co-administration of AAV vector and ImmTOR resulted in higher and more durable transgene expression after the first dose of gene therapy as well as robust inhibition of anti-AAV8 immunoglobulin G, or IgG and neutralizing antibodies. We believe the observation that co-administration of AAV vector and ImmTOR can lead to higher transgene expression illustrates the potential for dosing lower levels of AAV gene therapies when combined with ImmTOR. Integrating ImmTOR into a gene therapy protocol has the potential to provide a first dose benefit by enhancing liver-directed transgene expression and durability, as well as the potential to enable re-dosing to restore or augment transgene expression.

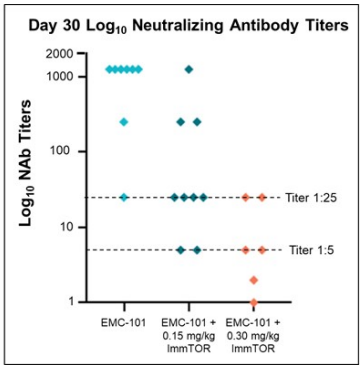
We have observed in preclinical studies that ImmTOR may also have hepatoprotective effects in mouse models of inflammation. As hepatotoxicity is associated with higher vector doses, one potential strategy that we are pursuing is to use ImmTOR to enable multiple lower doses of AAV vectors to mitigate toxicity risks associated with high vector

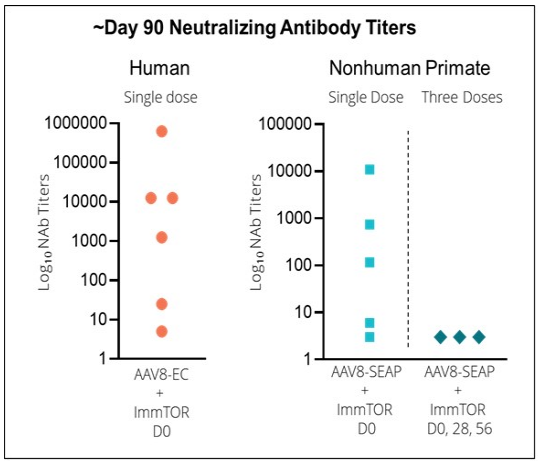
doses. We are concurrently working with our partner Ginkgo to develop a proprietary AAV capsid with improved transduction for liver-directed gene therapy. The below illustration depicts the potential benefits of ImmTOR in systemic AAV gene therapy.

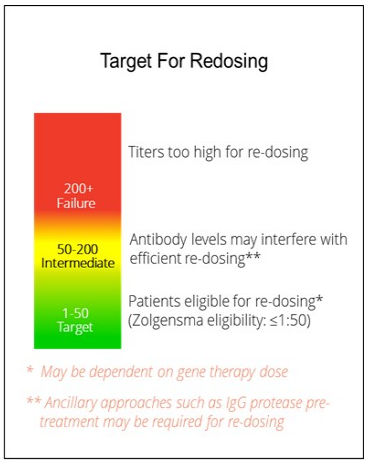


We recently completed a human proof-of-concept trial (SEL-399) in healthy volunteers who were treated with an empty AAV8 capsid (EMC-101), which is an AAV capsid containing no transgene, alone or in combination with ImmTOR. This clinical trial was conducted in Belgium in partnership with Asklepios BioPharmaceutical, Inc., or AskBio (a Bayer AG subsidiary). The goal of the SEL-399 clinical trial was to evaluate the appropriate dose of ImmTOR in humans to mitigate the formation of antibodies to AAV capsids used in gene therapies. Top-line results indicated that AAV8 empty capsids elicited peak median anti-AA8 neutralizing antibody, or NAb, titers of 1:6875. Median day 30 NAb titers were reduced to titers of 1:25 and 1:5 in the 0.15 mg/kg and 0.3 mg/kg ImmTOR cohorts, respectively, representing a 50-fold and 250-fold difference, respectively, compared to the median of control subjects dosed with AAV8 empty capsid alone, as depicted in the figure below. Further, we observed that at Day 30, six of six, or 100%, of subjects that received 0.3 mg/kg exhibited NAb titers of 1:25 or less, and four of six, or 67%, of those subjects at this dose exhibited NAb titers of 1:5 or less. We observed at Day 30 that six of nine, or 67%, of subjects that received 0.15 mg/kg of ImmTOR exhibited NAb titers of 1:25 or less, and two of nine, or 22%, of subjects at this dose had a titer of 1:5 or less. At Day 90, two of six subjects in the 0.3 mg/kg cohort were observed to have sustained control of neutralizing antibodies with titers of 1:25 or less. Consistent with preclinical data, we observed that the single dose ImmTOR cohorts showed delayed formation of neutralizing antibodies which eventually reached similar median levels of neutralizing antibodies to the control group by Day 90. Similar data were observed in NHP receiving a single dose of ImmTOR with an AAV gene therapy vector in a preclinical study. Importantly, we observed that two additional doses of ImmTOR, or a total of three monthly doses, provided durable inhibition of neutralizing antibodies in NHP. Although we could not evaluate three-monthly doses of ImmTOR in healthy volunteers, we intend to employ a three-monthly dose regimen in clinical trials performed in patients. ImmTOR showed safety results consistent with prior human studies and was generally well tolerated. No serious adverse events were reported. The most common treatment-related adverse events included mild-to-moderate stomatitis and rash. We believe this promising trial in healthy volunteers provides support for the potential use of ImmTOR for the inhibition of neutralizing antibodies to AAV8 in gene therapy clinical trials. The following graphs depict the effect of ImmTOR on the formation of neutralizing antibodies to AAV8 capsid in humans and NHP.









Finally, pre-existing neutralizing antibodies, which develop as a result of prior infection with wildtype AAV, are a major exclusion factor in clinical trials causing many potential patients to be ineligible for gene therapy. We have licensed a bacterial IgG protease, or Xork, from Genovis AB (publ.), or Genovis. IgG proteases have been shown by others to transiently cleave IgG and enable dosing of AAV vectors in the presence of pre-existing antibodies in NHP. However, IgG proteases, being of bacterial origin, are themselves immunogenic. The most commonly studied IgG protease, called IdeS or imlifidase, is derived from Streptococcus pyogenes, a common human pathogen. Most healthy individuals have been exposed to S. pyogenes and have pre-existing antibodies against IdeS. We believe that Xork is a differentiated product candidate, as it is derived from a Streptoccocal species that does not infect humans and so the enzyme shows very low cross reactivity to naturally existing antibodies in most human serum. We plan to develop Xork with the intention of enabling access to AAV gene therapy for those patients who are currently excluded due to pre-existing anti-AAV antibodies.

Through our analysis of genetic diseases, we have identified applications and patient segments that we believe would benefit from our ImmTOR platform. Our initial area of focus is on genetic metabolic diseases but may also include lysosomal storage diseases and genetic muscular diseases. We believe we are the first company to systematically pursue the development of AAV gene therapy product candidates with the goal of enabling repeat administration. We have engaged third parties with experience in gene therapy and rare diseases to support the development of our proprietary products. We also have licensed our ImmTOR platform to AskBio, Sarepta Therapeutics, Inc., or Sarepta, and Takeda Pharmaceuticals USA, Inc., or Takeda, for certain pre-specified targets.

Tolerogenic Therapies for Autoimmune Disease*:* Autoimmune diseases are caused by a breakdown in natural tolerance to our own self-antigens. With over 24 million Americans afflicted with autoimmune diseases, there is a large unmet medical need. As the ImmTOR platform is designed to induce or expand antigen specific T regulatory cells, we believe the ImmTOR platform has the potential to treat autoimmune diseases by restoring self-tolerance to auto-antigens.

Recent preclinical data generated by our scientific team suggest that ImmTOR may have profound synergistic activity with engineered IL-2 molecules that are selective for Tregs. The IL-2 pathway influences critical aspects of both immune stimulation and immune regulation. Tregs express a high affinity form of the IL-2 receptor. Low doses of IL-2 have been shown by others to selectively activate Tregs resulting in expansion of pre-existing Tregs. Clinical trials of

low dose IL-2 have shown evidence of efficacy in small clinical trials of autoimmune diseases, such as systemic lupus erythematosus. Other investigators have shown that IL-2 can be engineered to selectively bind the high affinity IL-2 receptor and expand pre-existing Tregs.

In our preclinical studies, we observed that ImmTOR combined with a Treg-selective IL-2 mutant protein, or IL-2 mutein, exhibited substantial synergistic activity in increasing the percentage and durability of total Treg expansion in the spleen. We believe that this combination has the potential to be a best-in-class therapy in diseases where expansion of total Treg may prove beneficial. Furthermore, in our preclinical studies, when we combined ImmTOR-IL with an antigen, we measured an approximately three-fold increase in antigen-specific T regulatory cells vs ImmTOR alone.

Our first program in autoimmune diseases is in primary biliary cholangitis, or PBC. PBC has a significant unmet medical need and a well-defined target antigen.

Our Product Candidates

Below is a summary of our ongoing discovery, research, and development programs:

Program	Phase of Development	Anticipated Next Steps	Commercial Rights
Biologic Therapies			
SEL-212 (Chronic Refractory Gout)	Phase 3 clinical trials (DISSOLVE I / DISSOLVE II)	Top-line data Q4 2022	Sobi
IgA nephropathy	Preclinical	IND enabling studies, 2022	Selecta
Gene Therapies			
Methylmalonic acidemia (MMA)	IND filed / Phase 1	IND approval and study commencement, 2022	Selecta
Ornithine Transcarbamylase (OTC) Deficiency	IND-enabling	Currently paused	Selecta
IgG protease (Xork)	Preclinical	IND enabling studies, 2022	Selecta
Pompe disease	Preclinical	Plans to be announced by our collaborator	AskBio
Duchenne muscular dystrophy (DMD)	Preclinical	Plans to be announced by our collaborator	Sarepta
Limb-girdle muscular dystrophy (LGMD)	Preclinical	Plans to be announced by our collaborator	Sarepta
Two indications for lysosomal storage disorders	Preclinical	Plans to be announced by our collaborator	Takeda
Tolerogenic Therapies for Autoimmune Disease			
Proprietary IL-2 receptor agonist	Preclinical		Selecta
Primary biliary cholangitis (PBC)	Preclinical		Selecta

Biologic Therapies – Chronic Refractory Gout

SEL-212 consists of ImmTOR co-administered with pegadricase. Our pegadricase consists of a yeast-derived uricase modified with PEG. Uricase is an enzyme endogenous to all mammals, except for humans and certain primates, which converts uric acid to the more soluble metabolite, allantoin. There is a natural limit to the amount of uric acid that can be excreted by the kidneys, which decreases with age and can be reduced by some medications. By converting uric acid to allantoin, uricase provides an additional way for the body to reduce uric acid.

Pegadricase is designed for the treatment of patients with chronic gout, refractory to standard uric acid lowering treatment, by breaking down the excess serum uric acid, or sUA, to the more soluble allantoin. However, the immune response to

pegadricase limits administration to a single dose which is effective for less than one month. The addition of ImmTOR to pegadricase (SEL-212) allows multiple monthly doses to be administered, thus reducing uric acid for a prolonged time.

In preclinical studies and in our Phase 1b and Phase 2 clinical trials, we observed that ImmTOR, when co-administered with pegadricase, SEL-212 substantially reduced the formation of associated ADAs. We believe that SEL-212 serves as proof of concept for the ImmTOR platform in ameliorating the unwanted immune response to an immunogenic biologic. SEL-212 is in two pivotal Phase 3 studies versus placebo, which we refer to as DISSOLVE I and DISSOLVE II, with top-line data expected in the fourth quarter of 2022. SEL-212 has been licensed (except as to Greater China) to Sobi, pursuant to our license and development agreement dated June 11, 2020, with Sobi, or the Sobi License.

Enrollment into the DISSOLVE II trial is ongoing and the study is being conducted in the United States and four countries across eastern Europe. As a result of the ongoing and rapidly evolving geopolitical situation in Ukraine and Russia, we have proactively undertaken mitigation steps to prioritize the safety of our patients and investigators, as well as address any potential disruptions. While we have temporarily closed screening and randomization at sites in both Russia and Ukraine, we have added 11 sites in the United States to further enrollment in DISSOLVE II. Out of these additional enrollment sites, nine have been activated and two are pending initiation, with activation expected imminently. Subject to ongoing geopolitical developments, we believe we remain on track to report data in the fourth quarter of 2022, and we will continue to work closely with our partner Sobi, clinical trial providers and regulatory authorities to evaluate any potential delays or adjustments to the timeline of the trial as a result of the circumstances.

The market for gout therapy

Gout is a painful and potentially disabling form of arthritis associated with elevation of sUA levels caused by an overproduction of uric acid and/or an inability of the kidneys to excrete adequate amounts of uric acid from the body. High concentrations of sUA lead to formation of uric acid crystals in joints and tissues, causing pain, inflammation and joint damage, and increase the risk for other conditions, including cardiovascular, cardiometabolic, joint and kidney disease.

Patients who are unable to reduce their sUA levels below 6.0 mg/dL with oral drugs are defined as having refractory gout. Chronic refractory gout constitutes a subset of gout patients exhibiting chronic high sUA levels and painful and damaging uric acid deposits. We estimate that there are approximately 160,000 chronic refractory gout patients in the U.S.

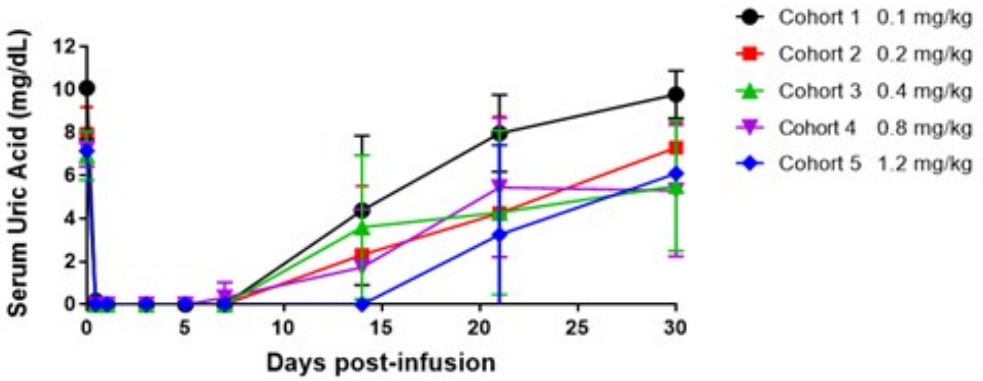
We believe SEL-212 may potentially address several key unmet needs in the treatment of chronic refractory gout: the durable control of sUA levels, the elimination of painful and damaging uric acid deposits, reduction in incidence and severity of flares, based on our preclinical studies, clinical trials, and market research. SEL-212 is designed to address these unmet medical needs while improving the dosing regimen to a once-monthly treatment.

SEL-212 Clinical Development

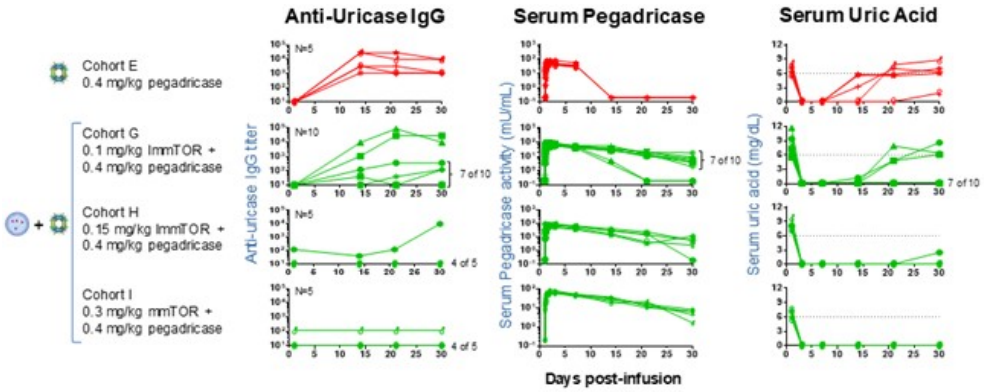
We conducted Phase 1a, Phase 1b, and Phase 2 clinical trials for SEL-212 at multiple sites in the United States. These trials were designed to demonstrate the induction of an immune response to pegadricase and the ability of ImmTOR to mitigate that immune response to both single and multiple doses. The table below summarizes the trial designs and objectives of these clinical trials.

	Design	Objective
Phase 1a SEL-212/101	• Subjects with hyperuricemia • Single dose of pegadricase • n=22	• Evaluate safety and tolerability • Define dose of pegadricase that would support monthly dosing • Demonstrate formation of ADAs
Phase 1b SEL-212/101	• Subjects with hyperuricemia • Single dose of SEL-212 • n=53	• Evaluate safety and tolerability • Proof-of-biological activity: • Mitigation of ADAs after single dose • Select dose to take forward into Phase 2
Phase 2 SEL-212/201	• Subjects with symptomatic gout and hyperuricemia • Repeated monthly dosing of SEL -212 • n=152	• Evaluate safety and tolerability • Clinical proof-of-concept: • Demonstrate sustained reduction of SUA with repeat dosing • Select dose to take into Phase 3

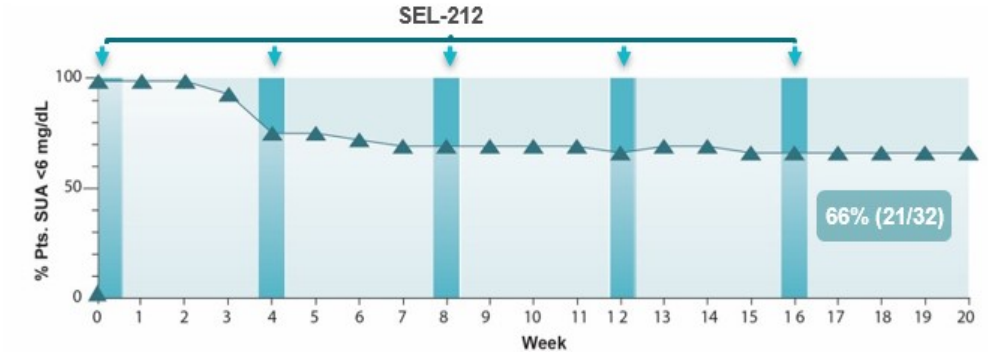
In the Phase 1a trial, we observed that a single dose of pegadricase rapidly reduced SUA levels below 6.0 mg/dL for each dose level, although SUA levels returned close to baseline by day 30. Consistent with our preclinical studies in animals, pegadricase induced uricase-specific ADAs in all patients with varying levels in this Phase 1a trial. The following table depicts the observations from the single ascending dose trial of pegadricase in patients with hyperuricemia. In this trial, patients with SUA > 6 mg/dL at screening were assigned to one of five cohorts receiving a single IV infusion of pegadricase (0.1, 0.2, 0.4, 0.8 or 1.2 mg/kg). Each cohort consisted of five patients, except for cohort 5 (1.2 mg/kg) which enrolled two patients.



In the Phase 1b clinical trial, we observed the potential for increasing doses of ImmTOR to mitigate the formation of pegadricase ADAs and sustain the anti-uricase enzyme activity through 30 days. The cohort of subjects who received a single 0.4 mg/kg dose of pegadricase alone showed development of uricase ADAs, a short pegadricase half-life, and poor control of SUA at 30 days. Three cohorts who received 0.4 mg/kg of pegadricase plus ascending doses of ImmTOR (0.1, 0.15 and 0.3 mg/kg) showed a dose related reduction in uricase ADAs, an increase in pegadricase half-life, and substantial reduction in SUA. This graphs below depict the observed correlation of SUA with anti-uricase IgG and serum pegadricase activity. In these graphs, anti-uricase IgG titers, serum pegadricase activity, and SUA are plotted against time for individual patients in cohorts A, G, H, and I. Each line represents an individual patient.



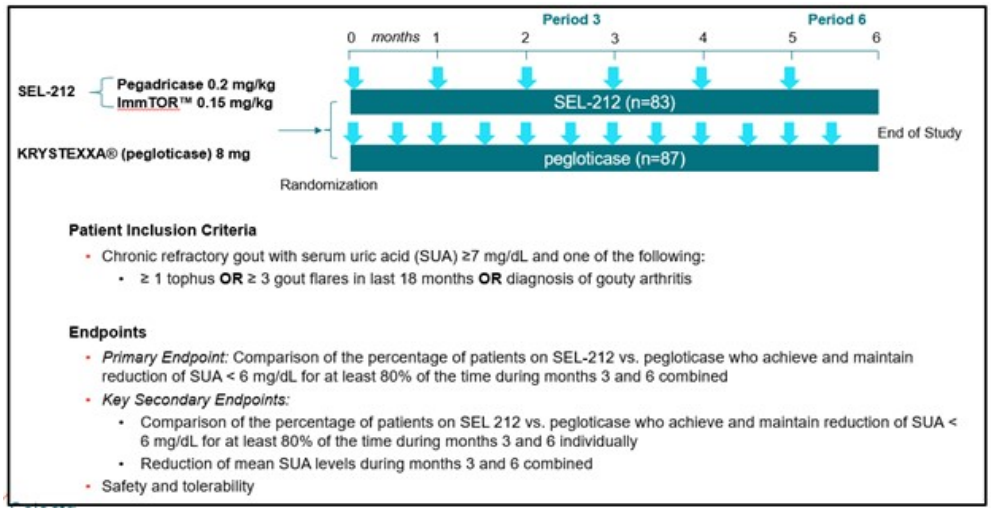
The Phase 2 trial included patients with symptomatic gout and elevated SUA levels in an open-label, multiple ascending-dose clinical trial of SEL-212 to demonstrate sustained reduction of SUA and identify the best dose for Phase 3. Five monthly doses of SEL-212 reduced SUA to less than 6.0 mg/dL in 21 of 32 patients, or 66%. In distinct contrast, pegadricase alone reduced SUA to less than 6.0 mg/dL in only three of 19 patients one month after a single injection (data from pegadricase alone cohorts from the SEL-037/101, SEL-212/101, and SEL-212/201 trials). We believe these results support our view that the addition of ImmTOR to pegadricase is able dramatically enhance the efficacy of pegadricase in the long-term reduction of SUA in gout patients. The chart below depicts SUA after five monthly doses of SEL-212.



We have observed that SEL-212 and its components, ImmTOR and pegadricase, were generally well-tolerated in the Phase 1a, 1b, and 2 clinical trials. In the Phase 1a trial we observed no serious adverse events, or SAEs, and that pegadricase was well tolerated at the five dose levels tested. Of the six SAEs in the Phase 1b trial, three were determined to not to be related to study drug by investigators. Of the remaining three SAEs that were determined to possibly or likely be related to study drug, two were cases of stomatitis that occurred at the highest dose of ImmTOR tested (0.5 mg/kg), leading us to define 0.3 mg/kg as the maximum tolerated dose of ImmTOR in this patient population. The remaining SAE was a case of drug hypersensitivity that occurred at a dose of 0.1 mg/kg of ImmTOR in combination with 0.4 mg/kg of pegadricase. In the Phase 2 trial, 20 subjects reported a total of 23 SAEs, nine in the five dose combination cohorts, seven of which were reported to be not related or unlikely related to study drug, and two of which were infusion reactions. All SAEs were successfully treated without residual effects.

Phase 2 head-to-head clinical trial

In March 2019, we initiated a non-registrational Phase 2 head-to-head clinical trial of SEL-212, which we refer to as COMPARE, in which SEL-212 was compared against the current FDA-approved therapy for chronic refractory gout, pegloticase, in multiple clinical sites in the United States.



In September 2020, we announced top-line results from the COMPARE trial. We observed a numerically higher response rate to pegloticase on the primary endpoint during months three and six combined but did not meet the primary endpoint of statistical superiority. SEL-212 did generate a statistically significant higher response rate of SEL-212 during the third month of treatment, as well as a statistically significant greater overall reduction in mean SUA levels in SEL-212 versus pegloticase in months three and six combined. We observed a numerically higher response rate of SEL-212 during the sixth month of treatment. In patients with tophi at baseline, we observed substantially higher responder rates for SEL-212 compared to pegloticase on the primary endpoint, and a statistically significant reduction in mean SUA levels when compared to pegloticase.

Approximately 41% of patients in the Phase 2 COMPARE trial had visible tophi at baseline, which is lower than we expected for the general refractory gout population. However, in these most severe patients with tophi, SEL-212 was superior to

pegloticase with a 58% responder rate for SEL-212 versus a 39 % responder rate for pegloticase. Response rates observed in patients with tophi at baseline are depicted below.

Evaluation Period (Month)	Data Set	SEL-212		pegloticase		Treatment Difference*		p****
		n*	Responder Percent**	n*	Responder Percent**	Absolute**	Relative***	
Month 3 and 6 combined	PP	26	58%	26	39%	19%	49%	0.085
	ITT	35	57%	34	41%	16%	39%	0.094

SEL-212 showed a favorable safety profile and was well-tolerated. There were no deaths during the study. There were no notable differences in serious TEAEs, treatment-related serious TEAEs, or infusion reactions between the two groups. A full analysis of safety signals, including gout flare incidence and severity, requires evaluation of the full data set and will be reported together with the full efficacy analysis in a manuscript in a medical journal.

Phase 3 DISSOLVE clinical program

In September 2020, we commenced the Phase 3 clinical program of SEL-212, which we refer to as DISSOLVE. We are responsible for the execution of the DISSOLVE program and are being reimbursed by Sobi on a quarterly basis for expenses incurred in connection with these activities. The Phase 3 clinical program consists of two double-blinded, placebo-controlled trials of SEL-212. We refer to these trials as DISSOLVE I and DISSOLVE II. Each trial is expected to enroll up to 120 patients, with up to 40 patients receiving 0.1 mg/kg of ImmTOR and 0.2 mg/kg of pegadricase, up to 40 patients receiving 0.15 mg/kg of ImmTOR and 0.2 mg/kg of pegadricase, and up to 40 patients receiving placebo. An additional 15 patients were added to the study sample size to account for potential treatment discontinuations that may occur due to the ongoing COVID-19 pandemic as a result of the emergence of COVID-19 variants which were not accounted for in the sample size calculations.

We commenced enrollment of DISSOLVE I in September 2020 and DISSOLVE II in December 2020. In December 2021, we announced the completion of enrollment of the DISSOLVE I trial. DISSOLVE I has a six-month primary endpoint followed by a six-month safety extension. DISSOLVE II will have a six-month primary endpoint with no extension. The primary endpoint of the DISSOLVE program is the maintenance of sUA levels below 6 mg/dL at six months. We currently expect that topline data from the Phase 3 DISSOLVE clinical program is expected in the fourth quarter of 2022.

Enrollment into the DISSOLVE II trial is ongoing and the study is being conducted in the United States and four countries across eastern Europe. As a result of the ongoing and rapidly evolving geopolitical situation in Ukraine and Russia, we have proactively undertaken mitigation steps to prioritize the safety of our patients and investigators, as well as address any potential disruptions. While we have temporarily closed screening and randomization at sites in both Russia and Ukraine, we have added 11 sites in the United States to further enrollment in DISSOLVE II. Out of these additional enrollment sites, nine have been activated and two are pending initiation, with activation expected imminently. Subject to ongoing geopolitical developments, we currently believe we remain on track to report data in the fourth quarter of 2022, and we will continue to work closely with our partner Sobi, clinical trial providers and regulatory authorities to evaluate any potential delays or adjustments to the timeline of the trial as a result of the circumstances.

Biologic Therapies – IgA Nephropathy

The second indication in our biologic therapies program is IgA nephropathy, an autoimmune kidney disease that occurs when immune complexes of a subclass of antibodies called immunoglobulin A1, or IgA1, accumulates in the kidneys. Previous studies in animal models conducted at independent laboratories demonstrated that bacterial IgA protease has the potential to remove injurious IgA immune complexes from kidneys and reduce inflammation, fibrosis, and hematuria. We believe these results suggest that IgA protease can potentially decrease the rate of disease progression and possibly even reverse the disease. The barrier to IgA protease commercialization has been the bacterial origin of the protease, which makes it highly immunogenic.

In clinical trials, we have observed ImmTOR mitigating the formation of ADAs to immunogenic enzymes. We intend to combine an IgA protease with our ImmTOR platform to develop a novel combination product candidate for the treatment of IgA nephropathy and IgA-mediated diseases.

In October 2020, we entered into an Option and License Agreement, or the IGAN Agreement, with IGAN Biosciences, Inc., or IGAN. Pursuant to the IGAN Agreement, IGAN granted us an exclusive license to research, evaluate, and conduct pre-clinical development activities on IGAN's proprietary IgA proteases. We have an option term of 24 months, during which we can elect to obtain an exclusive license to further develop and commercialize the product candidate to treat all IgA-mediated diseases, including IgA nephropathy, Linear IgA bullous dermatitis, IgA pemphigus, and Henoch-Schonlein purpura (also known as IgA vasculitis).

In October of 2021 we entered into a Collaboration and License Agreement, or the First Ginkgo Agreement, with Ginkgo. Pursuant to the First Ginkgo Agreement, Ginkgo will leverage their high throughput enzyme discovery, design and screening capabilities to identify and further optimize a proprietary, next generation IgA protease. We have an exclusive license to further develop and commercialize the discovered IgA proteases to treat all IgA-mediated diseases, including IgA nephropathy, Linear IgA bullous dermatitis, IgA pemphigus, and Henoch-Schonlein purpura.

These collaborations build on extensive preclinical as well as strong clinical data from our Phase 2 COMPARE trial for the treatment of chronic refractory gout that we believe further supports ImmTOR's potential for sustained therapeutic benefit when combined with immunogenic enzymatic therapies.

We are continuing to perform pre-clinical IND enabling studies.

Gene Therapies – Methylmalonic Acidemia

Our lead therapeutic gene therapy program, SEL-302, is intended to use ImmTOR to enhance the treatment of methylmalonic acidemia, or MMA, an inherited disorder in which the body is unable to process certain proteins and fats (lipids) properly. This program was previously being conducted under our collaboration with AskBio. In October and November 2020, we received rare pediatric disease designation and orphan drug designation, respectively, from the FDA for MMA-101, for the treatment of MMA due to methylmalonyl-CoA mutase, or MMUT gene mutations. See "——Licenses and Collaborations ——AskBio" for more information. In April 2021, we were notified by AskBio that it intended to opt-out of development of the MMA indication. The feasibility study and license agreement with AskBio, or AskBio Collaboration Agreement, otherwise remains in effect. Manufacturing of a new lot has been completed and is currently undergoing final release testing. We filed an IND to conduct a Phase 1/2 clinical trial of SEL-302 in pediatric patients with methylmalonic acidemia in the third quarter of 2021. On November 23, 2021, this trial was placed on clinical hold by the FDA, with questions specifically relating to chemistry, manufacturing and controls, or CMC, of the AAV vector. On February 9, 2022, we submitted a written response to the FDA to answer its questions. On March 9, 2022, we received a letter from the FDA indicating the clinical hold was removed and the trial may proceed.

Gene Therapies – OTC Deficiency

Our second proprietary gene therapy product candidate, SEL-313, is being developed to treat ornithine transcarbamylase, or OTC deficiency, and is currently in preclinical development. OTC deficiency is a rare genetic disorder that causes ammonia to accumulate in the blood due to mutations in the OTC gene, which is critical for proper function of the urea cycle. The most severe form of the disorder presents within the first few days of life. Severe symptoms include inability to control body temperature and breathing rate, seizures, coma, developmental delays and intellectual disability. Less severe forms of the disorder are characterized by delirium, erratic behavior, aversion to high protein foods, vomiting and seizures. The development of this program is currently paused.

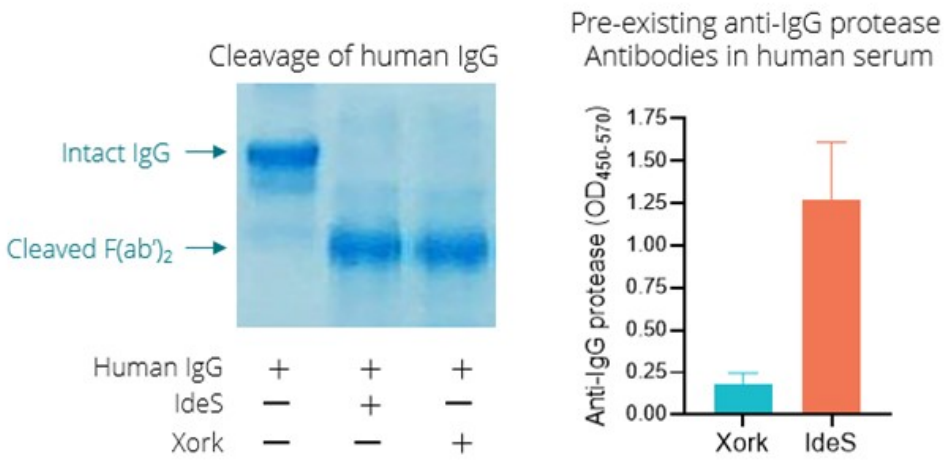
Gene Therapies – Xork

We have exclusively licensed Xork, an IgG-specific protease from Genovis, an enzyme technology company. We plan to develop Xork, either alone or in combination with our ImmTOR platform, with the goal of enabling the dosing of transformative gene therapies in patients with pre-existing AAV immunity due to natural exposures to AAV viruses. Currently, significant proportions of the potential patient populations for many gene therapy trials are ineligible for treatment by AAV mediated gene therapies due to pre-existing antibodies which limits transduction efficiency of the therapy and could trigger potentially dangerous immune responses.

Because of this, the commercial potential of many gene therapies may be significantly limited due to the ineligibility of large segments of the target patient population. This is particularly important for gene therapies given the low incidence and small prevalent populations of rare monogenic diseases which many gene therapies target. Patients that are ineligible for gene therapy due to pre-existing immunity may have few or no alternative therapies available to them.

Xork, as a pre-treatment in advance of an AAV gene therapy, can potentially open a treatment window by cleaving the IgG antibodies and transiently reducing their concentration.

IgG proteases are bacterial proteins, which are themselves immunogenic. We believe that Xork is differentiated from other IgG proteases since it is not derived from a human pathogen and thus, exhibits low cross-reactivity with human sera. Additionally, to further reduce any potential immunogenicity of the Xork enzyme, we plan to explore the combination of Xork and ImmTOR. The following images depict how Xork cleaves human IgG specifically and efficiently, but shows low cross reactivity to human sera compared to IdeS, an IgG protease derived from the common human pathogen Streptococcus pyogenes.



We believe that the combination of Xork and ImmTOR has the potential to address two of the major challenges to AAV gene therapy, pre-existing immunity that limits eligibility and de novo immunogenicity that can adversely affect safety and durability and which prevents the ability to re-dose AAV. We plan to explore the application of Xork in combination with our wholly owned gene therapies, as well as explore partnering opportunities for the enzyme with other gene therapy companies.

Tolerogenic Therapies for Autoimmune Disease – ImmTOR & ImmTOR-IL

We intend to apply our ImmTOR platform to treat autoimmune diseases. In preclinical studies, we have observed ImmTOR's ability to induce antigen-specific T regulatory cells. We believe that ImmTOR, in combination with an autoantigen of interest, could create self-tolerance to auto-antigens and thus be a novel approach to the treatment of autoimmune diseases.

Additionally, in preclinical studies we have observed ImmTOR, in combination with IL-2 muteins, expanding T-regulatory cells beyond IL-2 alone and we intend to pursue a combination of ImmTOR and IL-2 (ImmTOR-IL) in diseases where general T cell expansion has shown a therapeutic benefit. Additionally, in our preclinical data we have observed a three-fold increase in antigen specific regulatory T cells when ImmTOR and IL-2 is combined with an antigen of interest. We intend to pursue and develop treatments for autoimmune diseases with well-defined antigens using either ImmTOR or ImmTOR-IL.

Cyrus Biotechnology, Inc., a collaboration partner, is engineering a proprietary IL-2 protein to combine with the ImmTOR platform to potentially mitigate unwanted immune responses by reducing the inherent immunogenicity of the protein while also promoting immune tolerance. The IL-2 pathway influences critical aspects of both immune stimulation and immune regulation, through the development and expansion of Treg cells. These Treg cells are a specialized subpopulation of T cells involved in suppressing certain immune responses and maintaining the body's self-tolerance. In preclinical studies investigating the effects of ImmTOR in combination with a Treg-selective IL-2 mutant protein, or IL-2 mutein, we have observed a substantial synergistic activity in increasing the percentage and durability of Treg expansion in the spleen.

Our lead autoimmune diseases indication is PBC, a T cell driven autoimmune disease that causes progressive destruction of the bile ducts. Patients with PBC are in need of a highly targeted, liver-directed approach to treating the root cause of the disorder. We believe PBC has a well-defined target antigen, significant unmet medical need, and is well suited to the application of our ImmTOR immune tolerance platform, as preclinical data suggest that ImmTOR has the potential to enhance the tolerogenic environment in the liver and provide a hepatoprotective benefit.

Licenses and Collaborations

We intend to both partner and strategically out-license ImmTOR, ImmTOR-IL and Xork for use with other products that are outside our focus to larger biopharmaceutical companies. We believe our ImmTOR platform may also be of interest to biopharmaceutical companies with novel biologic development concepts or product candidates in clinical development that have demonstrated initial efficacy but are experiencing issues with safety or sustained efficacy due to inhibitory ADAs. Additionally, we may strategically in-license products to combine with ImmTOR and develop novel therapeutic products independently. Our key partnerships are listed below.

In-licenses

Ginkgo Bioworks Holdings, Inc.

On October 25, 2021, we entered into the First Ginkgo Agreement with Ginkgo. Under the First Ginkgo Agreement, Ginkgo will design next generation IgA proteases with potentially transformative therapeutic potential. In return, Ginkgo is eligible to earn both upfront research and development fees and milestone payments, including certain milestone payments in the form of our common stock, clinical and commercial milestone payments of up to $85 million in cash, as well as downstream value in the form of royalties on sales.

On January 3, 2022, we entered into a Collaboration and License Agreement, or the Second Ginkgo Agreement, with Ginkgo. Under the Second Ginkgo Agreement, we will engage with Ginkgo to design novel AAV capsids with potentially improved transduction, enhanced tissue tropism and reduced immunogenicity. In return, Ginkgo is eligible to earn both upfront research and development fees and milestone payments, including certain milestone payments in the form of our common stock, clinical and commercial milestone payments of up to $207 million in cash for each of a specified number of products which have the potential to total, in the aggregate, up to $1.1 billion. Ginkgo is also entitled to potential further downstream value in the form of royalties on sales.

Genovis

On October 21, 2021, we entered into a strategic licensing agreement with Genovis, or the Genovis Agreement. Under the Genovis Agreement, we paid to Genovis an upfront payment in exchange for an exclusive license to Genovis' Xork enzyme technology for all therapeutic uses in humans, excluding research, preclinical, diagnostic, and other potential non-therapeutic applications of the enzyme. Genovis is eligible to earn development and sales-based milestones, as well as tiered royalties on worldwide sales in the low double digits.

Cyrus Biotechnology, Inc.

On September 7, 2021, we entered into a Collaboration and License Agreement with Cyrus, or the Cyrus Agreement, pursuant to which Cyrus agreed to grant us an exclusive, worldwide license to certain intellectual property in order to form a protein engineering collaboration combining the ImmTOR platform with Cyrus' engineered protein therapeutics. We expect that novel engineered protein therapeutic candidates from the partnership will be used to expand our proprietary pipeline and further bolster the ImmTOR platform. In return for the licensed intellectual property, we made an upfront payment and will pay certain discovery, development, and sales-based milestones which could potentially total up to approximately $1.5 billion across multiple programs.

IGAN Biosciences

In October 2020, we entered into the IGAN Agreement. Pursuant to the IGAN Agreement, IGAN granted us an exclusive license to research, evaluate, and conduct preclinical development activities on IGAN's proprietary IgA proteases. We have an option term of 24 months, or the Option Term, during which we can elect to obtain an exclusive license to further develop and commercialize the product to treat all IgA-mediated diseases, including IgA nephropathy, Linear IgA bullous dermatitis, IgA pemphigus, and Henoch-Schonlein purpura.

Upon execution of the IGAN Agreement, we paid IGAN a one-time upfront payment of $0.5 million and we would owe additional payments to IGAN if we were to opt-in to an exclusive license agreement, as well as upon the achievement of certain development and sales milestones. During the Option Term, we may terminate the IGAN Agreement immediately for any reason upon written notice to IGAN. If we opt-in to an exclusive license agreement, we may terminate the IGAN Agreement upon 120 days' written notice.

Out-licenses

Takeda Pharmaceuticals USA, Inc.

On October 1, 2021, we entered into a strategic licensing agreement with Takeda, or the Takeda Agreement. Under the Takeda Agreement, we granted Takeda an exclusive license to our ImmTOR technology initially for two specified disease indications within the field of lysosomal storage disorders. Under the terms of the Takeda Agreement, we received an upfront payment and are entitled to receive up to $1.124 billion in future additional payments over the course of the partnership that are contingent on the achievement of development or commercial milestones or Takeda's election to continue its activities at specified development stages. We are also eligible for tiered royalties on future commercial sales of any licensed products.

Swedish Orphan Biovitrum

In June 2020, we announced that we had entered into the Sobi License, pursuant to which we agreed to grant Sobi an exclusive, worldwide (except as to Greater China) license to develop, manufacture and commercialize SEL-212, which is currently in development for the treatment of chronic refractory gout. In September 2020, pursuant to the Sobi License, Sobi paid us a one-time, upfront payment of $75 million. Sobi has also agreed to make milestone payments totaling up to $630

million to us upon the achievement of various development and regulatory milestones and sales thresholds for annual net sales of SEL-212, and tiered royalty payments ranging from the low double digits on the lowest sales tier to the high teens on the highest sales tier.

Additionally, Sobi purchased an aggregate of 5,416,390 shares of our common stock at a purchase price of $4.6156 per share for aggregate gross proceeds of $25 million, which we refer to as the Sobi Private Placement. The closing of the Sobi Private Placement occurred on July 31, 2020.

Under the Sobi License, we will have operational oversight of the Phase 3 DISSOLVE clinical program of SEL-212 (DISSOLVE I and DISSOLVE II) that commenced in September 2020, at Sobi's expense.

Sarepta Therapeutics

In June 2020, we entered into a research license and option agreement with Sarepta, or the Sarepta Agreement. Pursuant to the agreement, we granted Sarepta a license to research and evaluate ImmTOR in combination with Sarepta's AAV gene therapy or gene editing technology, using viral or non-viral delivery, or the Sarepta Product, to treat Duchenne Muscular Dystrophy and certain Limb-Girdle Muscular Dystrophy subtypes, or the Sarepta Indications. Sarepta will have an option term of 24 months during which it can opt-in to obtain an exclusive license to further develop and commercialize the Sarepta Product to treat at least one Sarepta Indication, with a potential to extend the option term if Sarepta pays an additional fee to us. Sarepta made an upfront payment to us upon signing of the agreement, and we are eligible to receive additional payments under the option term. If Sarepta opts-in to an exclusive license agreement, we could receive option exercise payments per indication and we would be entitled to significant development and commercial milestone payments and tiered royalties ranging from the mid-to-high single digits based on net sales. In June 2021, we received a payment of $3.0 million for the achievement of certain pre-clinical milestones.

AskBio

Feasibility Study and License Agreement

In August 2019, we entered into a feasibility study and license agreement with AskBio, or the AskBio Collaboration Agreement. The initial product candidate being developed under this collaboration is gene therapy for MMA which can cause severe developmental defects and premature death as a result of an accumulation of toxic metabolites. We previously conducted preclinical studies for this product candidate and will leverage that previous work within the collaboration. In April 2021, we were notified by AskBio that it intended to opt-out of development of the MMA indication. The feasibility study and license agreement with AskBio, or AskBio Collaboration Agreement, otherwise remains in effect. We filed an IND to conduct a Phase 1/2 clinical trial of our SEL-302 product candidate in pediatric patients with methylmalonic acidemia in the third quarter of 2021. On November 23, 2021, this trial was placed on clinical hold by the FDA, with questions specifically relating to CMC of the AAV vector. On February 9, 2022, we submitted a written response to the FDA to answer its questions. On March 9, 2022, we received a letter from the FDA indicating the clinical hold was removed and the trial may proceed. ImmTOR manufacturing, controlled by us, continues to proceed in accordance with our expectations and we have not observed any impact to any of our ImmTOR programs. In October and November 2020, we received rare pediatric disease designation and orphan drug designation, respectively, from the FDA for MMA-101, for the treatment of MMA due to methylmalonyl-CoA mutase, or MMUT gene mutations.

License Agreement for Pompe Disease

In December 2019, we entered into the AskBio License Agreement which provides AskBio with exclusive worldwide rights to our ImmTOR platform to research, develop and commercialize certain AAV-gene therapy products targeting the GAA gene, or derivatives thereof, to treat Pompe Disease. Pursuant to the AskBio License Agreement, AskBio paid us upfront fees of an aggregate of $7.0 million. Also pursuant to the AskBio License Agreement, AskBio agreed to make additional payments to us based on the achievement of certain development and commercial milestones of up to an aggregate of $237.0 million. AskBio will also be obligated to make tiered royalty payments to us at percentages in the mid-to-high single digits based on achievement of certain sales milestones.

We will supply AskBio with our ImmTOR platform and AskBio will be responsible for all preclinical, clinical and commercial manufacture and supply of products licensed under the AskBio License Agreement (other than ImmTOR) and carry out all other activities related to the research, development, and commercialization of such products at its sole expense, including all regulatory activities related thereto. The AskBio License Agreement contains other customary terms and conditions, including representations and warranties, covenants, termination, and indemnification obligations in favor of each party.

Massachusetts Institute of Technology

In 2008, we entered into a license agreement with the Massachusetts Institute of Technology, or MIT, which we refer to in its amended form as the MIT License. We amended the MIT License in January 2010, August 2013, November 2016, December 2019 and June 2020. Under the MIT License, we acquired an exclusive worldwide license, with the right to grant

sublicenses, to develop, make, sell, use and import certain licensed products that are therapeutic or prophylactic vaccines and use certain licensed processes in the exercise of rights to the licensed products, the manufacture, sale and practice of which are covered by patent rights owned or controlled by MIT, including patents jointly owned with Brigham and Women's Hospital, or Brigham, the President and Fellows of Harvard College, the Immune Disease Institute and the Children's Medical Center Corporation. Our exclusivity is subject to certain retained rights of these institutions and other third parties.

Upon our entry into the MIT License, we paid MIT a non-refundable license issue fee, reimbursed certain of MIT's costs and issued shares of our common stock to MIT and the other institutional patent owners which were subject to certain anti-dilution, registration and other protective rights. We are obligated to pay MIT creditable annual maintenance fees, low-single-digit running royalty on annual net sales, developmental milestones up to an aggregate of $1.5 million, a mid-single digit percentage of certain payments we receive from corporate partners and a specified percentage of certain income received from sublicensees after 2009 between 10% and 30%. We may terminate the MIT License at any time upon six months' written notice. MIT has the right to terminate the MIT License immediately upon written notice to us if we cease to carry on our business related to the MIT License, fail to maintain insurance as required under the MIT License, file for bankruptcy, fail to pay amounts due under the MIT License, challenge or assist others in bringing a challenge to MIT's patents or fail to cure material breach within 60 days' written notice thereof. Absent early termination, the MIT License will continue until the expiration or abandonment of the last to expire patent right subject to the MIT License.

In June 2020, we entered into a Fifth Amendment to the MIT License, or the MIT Amendment, which was effective as of May 15, 2020. Pursuant to the MIT Amendment, certain of our diligence obligations were extended to the second quarter of 2021, including a diligence obligation to commence a Phase 3 trial for a licensed product by a specific date in the second quarter of 2021. Additionally, certain of our development and regulatory milestones and payments upon achievement of such milestones were adjusted.

Shenyang Sunshine Pharmaceutical Co., Ltd.

In 2014, we entered into a license agreement with 3SBio, as amended in 2017, which we refer to as the 3SBio License. Pursuant to the 3SBio License, we were granted an exclusive license to certain pegadricase-related patents and related know-how owned or in-licensed by 3SBio for the worldwide (except for Greater China and Japan) development and commercialization of products based thereupon for human therapeutic, diagnostic and prophylactic use. We are also granted a worldwide (except for Greater China) exclusive license to develop, commercialize and manufacture or have manufactured products combining our proprietary ImmTOR platform with pegadricase or related compounds supplied by 3SBio (or otherwise supplied if our rights to manufacture are in effect) for human therapeutic, diagnostic and prophylactic use. We were also granted a co-exclusive license to manufacture and have manufactured pegadricase and related compounds for our preclinical and clinical use or, if the 3SBio License is terminated for 3SBio's material breach, for any use under the 3SBio License. In addition, the 3SBio License, as amended, permits us to utilize one or more third parties to provide up to 20% of our commercial supply of pegadricase. Otherwise, except in the case of a supply shortage on the part of 3SBio, we are obligated to obtain at least 80% of our supply of such compounds for Phase 3 clinical trials and commercial use from 3SBio under the terms of our separate Commercial Supply Agreement with 3SBio dated August 1, 2019.

Under the 3SBio License we have paid to 3SBio an aggregate of $7.0 million in upfront and milestone-based payments. We are required to make future payments to 3SBio contingent upon the occurrence of events related to the achievement of clinical and regulatory approval milestones of up to an aggregate of $15.0 million for products containing our ImmTOR platform. We are also required to pay 3SBio tiered royalties on annual worldwide net sales related to the pegadricase component of products at percentages ranging from the low-to-mid single digits for products containing our ImmTOR platform, subject to specified reductions. These royalties are payable, on a country-by-country and product-by-product basis until the later of (i) the date that all of the patent rights for that product have expired in that country or (ii) a specified number of years from the first commercial sale of such product in such country.

The 3SBio License expires on the date of expiration of all of our royalty payment obligations unless earlier terminated by either party for an uncured material default of the other party or for the other party's bankruptcy. We may also terminate the 3SBio License on a country-by-country or product-by-product basis for any reason effective upon 60 days' prior written notice to 3SBio or, with respect to a given product, immediately upon written notice to 3SBio if we identify a safety or efficacy concern related to such product.

Manufacturing

We manufacture ImmTOR using a scalable, self-assembly nanoemulsion process with well-defined, pharmaceutical unit operations. This proprietary, highly specialized and precisely controlled manufacturing process enables us to reproducibly manufacture ImmTOR across many production scales, from milligram-scale at the laboratory bench to hundreds of grams to

multi-kilogram scale for commercial production. We have also developed and executed the required detailed analytic characterization of our products.

For our most advanced product candidate, SEL-212, we are producing ImmTOR at an approximately 400-gram scale process, which, at the doses being tested in the Phase 3 DISSOLVE program, we believe will be suitable for commercialization. The process is designed such that this same equipment is capable of potentially producing up to a one-kilogram batch size scale. As our nanoparticle manufacturing process is compact, and therefore also portable, our strategy is to transfer our custom designed process skids to a contract manufacturing organization, or CMO, and have the CMO produce the nanoparticles under our direction. This is the strategy we use for production of clinical supplies for clinical trials and would be the expected strategy for commercial production.

The pegadricase enzyme for SEL-212 is produced by fermentation in E. coli and is sourced from 3SBio in China. Through a licensing arrangement, we own exclusive worldwide rights to pegadricase outside of China, with co-ownership of rights in Japan and with 3SBio owning all rights in China. Under this arrangement, 3SBio has agreed to supply pegadricase for the SEL-212 program. There is also a second supplier for pegadricase in the United States.

Our AAV vector product candidates are produced using the established triple transfection production process at CMOs. We work closely with our CMOs who have platform AAV production processes that we are able to leverage for our specific AAV product candidates.

Intellectual Property

Our ImmTOR platform is designed to deliver precise instructions to the immune system as a result of the natural predisposition of the immune system to interrogate nanoparticles such as viruses. In connection with our founding, we licensed multiple patent families, including a patent family based in part on the pioneering research performed by our co-founders at Harvard University, MIT and Brigham. We have also conducted extensive research in-house to further research this area, leading to key discoveries regarding and uses for our ImmTOR technology. We have aggressively sought to extend and protect the proprietary intellectual property underlying the composition and use of ImmTOR, such as for antigen-specific immunotolerance.

We endeavor to protect our nanoparticle technology, which we consider fundamental to our business, by seeking, maintaining and defending patent and other intellectual property rights, whether developed internally or licensed from third parties, relating to our program, product candidates, their methods of use and the processes for their manufacture. Our practice is to strive to protect our intellectual property by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, programs and product candidates that are commercially important to the operation and growth of our business. We also rely on trade secrets and know-how relating to our proprietary technology, programs and product candidates, and continue innovating and seeking in-licensing opportunities to maintain, advance and fortify our proprietary position in our nanoparticle-based immunotherapy program and product candidates as well as to develop new programs and other product candidates. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology programs, inventions and improvements; to preserve the confidentiality of our trade secrets; to maintain our licenses to use intellectual property owned or controlled by third parties; to defend and enforce our proprietary rights, including our patents; and to operate without infringing the patents and proprietary rights of third parties.

We have developed and in-licensed numerous patents and patent applications and possess substantial know-how and trade secrets relating to our technology programs and product candidates. Our patent portfolio contains a number of issued patents in the United States and certain foreign jurisdictions. We also own a number of pending patent applications in the United States and certain foreign jurisdictions. These patents and patent applications include claims related to:

- tolerance immunotherapy programs;
- methods and compositions related to our proprietary nanoparticles in a variety of applications, including tolerance applications, such as:
    - mitigating anti-drug antibodies and/or their effects associated with protein drugs, such as for chronic refractory gout, including coverage for ImmTOR co-administered with pegadricase, which related patents are expected to expire between 2032 and 2041, and
    - genetic therapies (such as viral vector gene therapy), including coverage for ImmTOR co-administered with a viral vector, which related patents are expected to expire between 2032 and 2042; and
- development and commercialization of SEL-212, including both composition of matter and method of treatment claims (there are multiple patent families with claims that cover the SEL-212 product, one of which is a licensed, issued U.S. patent that expired in August 2021).

In addition, we have exclusively or non-exclusively licensed intellectual property, including U.S. issued patents, foreign issued patents, and pending applications in both the U.S. and foreign jurisdictions. The licensed patents and patent applications cover various aspects of the technology being developed by us, including claims directed to compositions of matter and methods of use, and have been filed in various countries worldwide including in North America, Europe and Asia, with material expiration dates varying to, if claims are issued, 2042. In addition to filing and prosecuting patent applications in the United States, we often file analogous patent applications in the European Union and in additional foreign countries where we believe such filing is likely to be beneficial, including but not limited to, Australia, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico and/or South Korea.

Each patent's term depends upon the laws of the countries in which they are obtained. The patent term in most countries in which we file is 20 years from the earliest date of filing of a non-provisional patent application. Notably, the term of U.S. patents may be extended due to delays incurred due to compliance with FDA or by delays encountered during prosecution that are caused by the USPTO. For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved drugs of up to five years beyond the expiration of the patent, depending upon the length of time the drug is under regulatory review. There is a limit to the amount of time a patent may be extended in the United States; no patent extension can extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar patent term extensions are available in Europe and other jurisdictions for patents that cover regulatory-approved drugs. Currently, we own or license patents and patent applications with expected material expiration dates ranging from 2032 to 2042. However, the actual patent protection period varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Product candidates that we successfully develop and commercialize may compete with existing therapies and new therapies that may become available in the future.

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of any other tolerance or immune modulation product candidates that we develop, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic or biosimilar products.

SEL-212 may compete with others in the gout market, including pegloticase, which contains a pegylated uricase similar to the pegadricase component of SEL-212 and is indicated for the treatment of refractory gout. Horizon Pharma plc, whose affiliates own pegloticase, may find other approaches to eliminate undesired immunogenicity to pegloticase. Long-term treatment with global immunosuppressive products may increase the susceptibility to contract infections, tumors and may lead to organ failure.

Large companies with active research to prevent the formation of ADAs and treat allergies or autoimmune diseases include Eli Lilly, Roche Holding AG, Sanofi S.A., Pfizer Inc., and Merck & Co., Inc. Small, early-stage biopharmaceutical companies active in the research for new technologies to induce antigen-specific immune tolerance include Anokion SA, Apitope International NV, Cour Pharmaceutical Development Company, Inc., Cue Biopharma, Dendright International, Inc., Parvus Therapeutics, REGiMMUNE Corporation, Rubius Therapeutics, Inc., Tolerion, Inc., Topas Therapeutics GmbH, SQZ Biotechnologies and Txcell SA. Biopharmaceutical companies active in the research for MMA include LogicBio, Poseida, and Moderna. Biopharmaceutical companies active in the research for Ornithine transcarbamylase include Ultragenyx, Poseida, TranslateBio, Arcturus, and Kaleido. Biopharmaceutical companies active in the research for IgA nephropathy include Omeros, Travere, EMD Serono, Novartis, Ionis, Visterra, Reata, and Alnylam. Biopharmaceutical companies active in the PBC research include Intercept Pharmaceuticals, Genfit, GenKyoTex, GSK, Eli Lilly, and CymaBay. Biopharmaceutical companies active in the IL-2 research include Roche Holding AG, Amgen, Bristol Myers Squibb, Eli Lilly, and Moderna.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing.

SEL-212 is subject to regulation in the United States as a combination product. If marketed individually, each component would be subject to different regulatory pathways and would require approval of independent marketing applications by the FDA. A combination product, however, is assigned to a Center that will have primary jurisdiction over its regulation based on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic action. In the case of SEL-212, we believe that the primary mode of action is attributable to the biologic component of the product. In the case of SEL-212, which we believe will be regulated as a therapeutic biologic, the FDA's Center for Drug Evaluation and Research, or CDER, will have primary jurisdiction over premarket development. We expect to seek approval of SEL-212 through a single BLA reviewed by CDER, and we do not expect that the FDA will require a separate marketing authorization for each constituent of SEL-212.

Biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. SEL-212 and any other product candidates that we develop must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries.

U.S. biological products development process

The process required by the FDA before a biologic, including a gene therapy, may be marketed in the United States is summarized below.

Biological product candidates are preclinically tested before any testing is done in humans. These tests, or non-clinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

The clinical study sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND which must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical study on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. In addition to these requirements, biological product candidates may also require evaluation and assessment by an institutional biosafety committee, or IBC, that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution.

Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, patient selection and exclusion criteria, and the parameters to be used to monitor patient safety. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical study must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical study will be conducted. Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product candidate is initially introduced into healthy human patients and tested for safety.
- Phase 2. The biological product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

The FDA or the sponsor or its data safety monitoring board may suspend a clinical study at any time on various grounds. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the biological product candidate has been associated with unexpected serious harm to patients.

Sponsors of clinical trials of FDA-regulated products, including biologics, are also required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Concurrent with clinical trials, companies must also finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements.

After the completion of clinical trials of a biological product candidate, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal trials, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act, or FDASIA, requires that sponsors planning to submit a BLA for a biological product that in certain circumstances n submit an initial Pediatric Study Plan, or PSP, within sixty days after a Type C meeting or as may be agreed between the sponsor and FDA. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Under the Prescription Drug Fee User Act, or PDUFA, as amended, each BLA must be accompanied by a user fee. Fee waiver or reductions are available under certain circumstances, including for the first application filed by a small business. In addition, no user fees are assessed on BLAs on products designated as orphan drugs unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA for completeness. The FDA may refuse to file any BLA that it deems incomplete or otherwise not reviewable and may request additional information. Once the submission is accepted for filing, the FDA substantively reviews the BLA to determine, among other things, whether the proposed product is safe, pure and potent, and manufactured in accordance with cGMP requirements. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a non-binding recommendation on approval. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product candidate. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities in which the product is manufactured to determine whether the manufacturing processes and facilities are in compliance with GMPs. The FDA may also audit the clinical investigation sites to determine that they have complied with good clinical practices.

Notwithstanding the submission of relevant data and information, the FDA may ultimately deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than the applicant interprets the same data. If the FDA denies approval of a BLA in its then-current form, the FDA will issue a complete response letter detailing deficiencies in the application. If a response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

One of the performance goals agreed to by the FDA under PDUFA is to review 90% of standard BLAs in 10 months from the filing date and 90% of priority BLAs in six months from the filing date, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs.

Orphan Designation

Prior to the submission of a BLA, the FDA may grant orphan designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the product for this type of disease or condition will be recovered from sales in the United States After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other application to market the same product for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approve orphan product. Competitors, however, may

receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

Rare Pediatric Disease Designation

The Rare Pediatric Disease designation program allows for a sponsor who receives an approval for a product to potentially qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new biological products that meet certain criteria. Specifically, new biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biologic may request that the FDA designate the biologic as a Fast Track product at any time during the clinical development of the product.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness compared to marketed products. Additionally, a product may be eligible for accelerated approval. Biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval, which means that they may be approved on the basis of studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a biological product subject to accelerated approval perform adequate and well-controlled post-marketing clinical studies to confirm such benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

In addition, under the provisions of FDASIA, the FDA established a Breakthrough Therapy Designation which is intended to expedite the development and review of products that treat serious or life-threatening diseases or conditions. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the features of Fast Track designation, as well as more intensive FDA interaction and guidance.

Post-approval Requirements

Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP requirements. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products include record-keeping requirements, reporting of adverse effects and reporting updated safety and efficacy information.

We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, or ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical study or studies. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. As a result, the ultimate impact, implementation and meaning of the BPCIA is subject to significant uncertainty.

Government Regulation outside of the United States

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries.

The requirements and process governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

In the European Economic Area, or EEA, which is composed of the 27 member states of the European Union plus Norway, Iceland and Liechtenstein medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA.

There are two types of MAs.

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), among others. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases. Under the accelerated procedure the standard 210 days review period is reduced to 150 days.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

To obtain regulatory approval of an investigational biological product under European Union regulatory systems, we must submit a marketing authorization application, which is similar to the U.S. BLA. The European Union also provides opportunities for market exclusivity. Upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity, which prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic or biosimilar application, and an additional two years of market exclusivity, during which no generic or biosimilar product can be marketed. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no marketing authorization application shall be accepted, and no marketing authorization shall be granted for a similar medicinal product for the same indication. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric

studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an “orphan medicinal product” in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for certain financial and exclusivity incentives.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

When conducting clinical trials in the EU, we must adhere to the provisions of the European Union Clinical Trials Directive (Directive 2001/20/EC) and the laws and regulations of the EU Member States implementing them. These provisions require, among other things, that the prior authorization of an Ethics Committee and the competent Member State authority is obtained before commencing the clinical trial. In 2014, the EU passed the Clinical Trials Regulation (Regulation 536/2014), which will replace the current Clinical Trials Directive, to ensure that the rules for clinical trials are identical throughout the European Union.

We are also subject to data privacy and security laws in the jurisdictions outside of the U.S. in which we are established, run clinical trials or in which we sell or market our products once approved. For example, in Europe we are subject to Regulation (EU) 2016/679 (General Data Protection Regulation or GDPR) in relation to our collection, control, processing and other use of personal data (i.e. data relating to an identifiable living individual). We process personal data in relation to participants in our clinical trials in the EEA., including the health and medical information of these participants. The GDPR is directly applicable in each E.U. Member State, however, it provides that E.U. Member States may introduce further conditions, including limitations which could limit our ability to collect, use and share personal data (including health and medical information), or could cause our compliance costs to increase, ultimately having an adverse impact on our business. The GDPR imposes accountability and transparency obligations regarding personal data. We are also subject to E.U. rules with respect to cross-border transfers of personal data out of the E.U. and EEA. We are subject to the supervision of local data protection authorities in those E.U. jurisdictions where we are established or otherwise subject to the GDPR. A breach of the GDPR could result in significant fines, regulatory investigations, reputational damage, orders to cease/ change our use of data, enforcement notices, as well potential civil claims including class action type litigation where individuals suffer harm. Moreover, the United Kingdom leaving the E.U. could also lead to further legislative and regulatory changes. It remains unclear how the United Kingdom data protection laws or regulations will develop in the medium to longer term and how data transfer to the United Kingdom from the E.U. will be regulated. However, the United Kingdom has transposed the GDPR into domestic law with the Data Protection Act 2018, which remains in force following the United Kingdom’s departure from the EU.

Other Healthcare Laws

The federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly (regardless of knowledge of this specific statute) and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. The majority of states also similar have anti-kickback laws, which in some cases are more restrictive.

The federal false claims and civil monetary penalties laws, including the civil False Claims Act, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation. A claim includes “any request or demand” for money or property presented to the U.S. government. Violation of the federal Anti-Kickback Statute may also constitute a false or fraudulent claim for purposes of the federal civil False Claims Act. Actions under the civil False Claims Act may be brought by the Department of Justice or as a qui tam action by a private individual in the name of the government. Violations of the civil False Claims Act can result in very significant monetary penalties and treble damages, and may be accompanied by additional civil monetary penalties against

individuals. Many states also have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The ACA imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH made HIPAA's security standards directly applicable to, as well as imposed certain other privacy obligations on, "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a).

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological products for which we obtain regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Sales of any products for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care plans, private health insurers and other organizations.

The process for determining whether a third-party payor will provide coverage for a pharmaceutical or biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a pharmaceutical or biological product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and, due to subsequent legislative amendments, will stay in effect through 2027 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and imaging centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Recently there has also been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed to, among other things, bring more transparency

to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies.

Human Capital Resources

At Selecta Biosciences, we consider human capital to be an essential driver of our business and successful strategy creation and execution. Our people, driven by our Collaborative, Pioneering, and Patient Focused culture, propel our business forward, strengthening us for long-term success.

As of December 31, 2021, we had 58 employees, 44 of whom are primarily engaged in research and development activities and 14 in corporate functions. 66% of our employees have at least one of a Masters, PhD, or MD degree. Our 2021 annualized voluntary turnover rate was 12.87%. All employees reside and work in the United States and are not represented by a labor union. We consider our employee relations to be strong and in good standing.

Our goal is to continually engage our talented and diverse workforce to drive value creation both for our business and ultimately our patient populations. We believe in a proactive approach to talent management focusing on retention of key talent, critical role successor identification, and impactful employment development. Additional priority areas intended to drive engagement include successful recruitment of diverse talent, continual promotion of professional development at all levels, introduction, and evolution of business-friendly HR solutions, coupled with an intentional culture dialog aimed to drive a high engagement, high performance, patient centric culture.

To further drive attraction and retention of our high-quality, experienced, and diverse workforce, we invest in the physical, emotional, and financial well-being of our employees. These investments include a competitive mix of compensation and generous insurance benefits. To assist employees with the rising cost of healthcare, we pay 100% of an employee’s deductible and co-insurance payments. All employees are eligible to participate in our equity compensation programs. All employees are awarded new hire equity and annual equity as well as the opportunity to participate in our Employee Stock Purchase Plan. Employees are also eligible to receive an annual cash bonus and to participate in a 401(k)-retirement plan with an industry competitive company match.

In response to the COVID-19 pandemic, we initially implemented changes to our business practices in March 2020, taking precautions to protect the health and safety of our employees by instituting robust hygiene practices, installing temporary safety structures, increasing our cleaning protocols, implementing weekly COVID-19 testing, and limiting regular access to our facilities. As the health environment continues to evolve, we remain committed to actively monitor and evolve our protocols to align with the Center for Disease Control’s best practices, including tracking vaccination and booster status and providing regular communication related to community resources. Additionally, we introduced wellness initiatives as well as a flexible work environment policy and enhanced remote technology solutions, providing remote work opportunities for all employees both now, and well into the future.

Available Information

We file electronically with the SEC our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements and other information. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. We make available on our website at www.selectabio.com, free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC. The hyperlink to our website is included as an inactive textual reference only, and the information on our website is not incorporated by reference in this Annual Report on Form 10-K or in any other filings we make with the SEC.

RISK FACTORS SUMMARY

Investing in our common stock involves various risks. You should carefully read and consider the matters discussed in this Annual Report under the heading "Risk Factors," which include the following risks:

- We are a clinical-stage company and have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We will need substantial additional funding in order to complete development of our product candidates and commercialize our products, if approved.
- The terms of our credit facility place restrictions on our operating and financial flexibility.
- Our product candidates are based on our ImmTOR platform, which is an unproven approach designed to induce antigen-specific immune tolerance to biologic drugs.
- Regulatory authorities in the United States and European Union have limited experience in reviewing and approving gene therapy products.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome.
- The COVID-19 pandemic may continue to adversely impact our business, including sourcing raw materials and supplies to produce our product candidates, our preclinical studies and clinical trials.
- Geopolitical events, instability and wars can adversely affect both our clinical operations and supply chains that we rely on to advance our drug candidates.
- We rely on 3SBio in China as our primary supplier of pegadricase and on other third parties for the manufacture of our product candidates for preclinical and clinical testing, and expect to continue to do so for the foreseeable future.
- We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including by failing to meet deadlines for the completion of such trials.
- If we or our licensors are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would negatively impact our business.
- We may suffer from effects of macroeconomic instability and inflation.
- We would be reliant on Sobi to execute the marketing and sale of SEL-212, if SEL-212 were approved.
- We may not have the funds necessary to fulfill our obligation to repurchase certain warrants.
- We are involved in two securities class action lawsuits.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should consider carefully the risks described below, together with the other information included or incorporated by reference in this Annual Report. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

Risks Related to our Financial Position and Need for Additional Capital

We are a development-stage company and have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses in every year. Our net losses were $25.7 million for the year ended December 31, 2021, and $68.9 million and $55.4 million for each of the years ended December 31, 2020 and 2019, respectively. As of December 31, 2021, we had an accumulated deficit of $430.3 million. To date, we have financed our operations primarily through public offerings and private placements of our securities, funding received from collaboration and license arrangements and our credit facility. We currently have no source of product revenue, and we do not expect to generate product revenue for the foreseeable future. We have devoted substantially all of our financial resources and efforts to developing our ImmTOR platform, identifying potential product candidates and conducting preclinical studies and our clinical

trials. We are in the early stages of development of most of our product candidates, and we have not completed development of any ImmTOR-enabled therapies. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We expect that our expenses will increase substantially as we:

- continue the research and development of our product candidates;
- seek to enhance and evolve our ImmTOR platform and discover and develop additional product candidates;
- seek to maintain and enter into collaboration, licensing and other agreements, including, but not limited to research and development, and/or commercialization agreements;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- potentially establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio, including through licensing arrangements;
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts;
- experience any delays or encounter any issues with any of the above, including, but not limited to, failed studies, complex results, safety issues or other regulatory, manufacturing or scale-up challenges; and
- are exposed to broad macroeconomic conditions including inflation and supply chain tightness which could result in us paying more, or being unable, to access goods and services.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval and securing reimbursement for these product candidates, manufacturing, marketing and selling any products for which we may obtain regulatory approval, and establishing and managing our collaborations at various stages of a product candidate's development. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical and biological product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA or other regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase and product revenue could be further delayed.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations.

We will need substantial additional funding in order to complete development of our product candidates and commercialize our products, if approved. If we are unable to raise capital when needed and on terms favorable to us, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to develop our gene therapy pipeline, including our collaboration with AskBio, research and develop our autoimmune programs and advance the evolution of our ImmTOR platform in combination with IL-2, and continue research and development for other product candidates. Additionally, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Accordingly, we will need to obtain substantial additional funding to continue operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our clinical trials, our other research and development programs or any future commercialization efforts.

We believe that our existing cash, cash equivalents and restricted cash as of December 31, 2021 will enable us to fund our current planned operations into the third quarter of 2023, though we may realize additional cash resources upon the achievement of certain contingent collaboration milestones or it may pursue additional cash resources through public or private equity or debt financings or by establishing collaborations with other companies. Management's expectations with respect to our ability to fund current and long-term planned operations are based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, we may need to seek additional strategic or financing opportunities sooner than would otherwise be expected. However, there is no guarantee that any collaboration milestones will be achieved or that any of these strategic or financing opportunities will be executed on favorable terms, and some could be dilutive to existing stockholders. If we are unable to obtain additional funding on a timely basis, we may be forced to significantly curtail, delay, or

discontinue one or more of its planned research or development programs or be unable to expand our operations, meet long-term obligations or otherwise capitalize on our commercialization of our product candidates. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of our clinical trials, preclinical development, and laboratory testing;
- the number of product candidates that we pursue and the speed with which we pursue development;
- our collaboration agreements remaining in effect, our entering into additional collaboration agreements and our ability to achieve milestones under these agreements;
- our headcount growth and associated costs;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders, and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs, including our clinical trial programs, or the commercialization of any product candidates, or be unable to sustain or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

The terms of our credit facility place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

On August 31, 2020, we entered into a term loan, or the 2020 Term Loan, of up to $35.0 million, consisting of term loans in an aggregate amount of $25.0 million, or the Term A Loan, and term loans in an aggregate amount of $10.0 million, or the Term B Loan, governed by a loan and security agreement among us and Oxford Finance LLC, or Oxford, as collateral agent and a lender, and Silicon Valley Bank, or SVB, as a lender. The Term A Loan was funded in full on August 31, 2020, the proceeds of which were used to repay our previously existing 2017 term loan and for general corporate and working capital purposes, and the draw period relating to the Term B Loan expired on September 30, 2021.

The 2020 Term Loan is secured by a lien on substantially all of our assets, other than intellectual property, provided that such lien includes any rights to payments and proceeds from the sale, licensing or disposition of intellectual property. We also granted Oxford a negative pledge with respect to our intellectual property.

Failure to satisfy our current and future debt obligations, including covenants to take or avoid specific actions, under the 2020 Term Loan could result in an event of default, our lenders could accelerate all of the amounts due. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

Our ability to use our net operating loss and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

We have net operating loss carryforwards, or NOLs, for federal and state income tax purposes that may be available to offset our future taxable income, if any. In general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to use its pre-change NOLs to offset future taxable income. If the U.S. Internal Revenue Service, or IRS, challenges our analysis that existing NOLs will not expire before utilization due to previous ownership changes, or if we undergo an ownership change in connection with or after a public offering, our ability to use our NOLs could be limited by Section 382 of the Code. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Furthermore, our ability to use NOLs of companies that we may acquire in the future may be subject to limitations. As a result, we may not be able to use a material portion of the NOLs reflected on our balance sheet, even if we attain profitability. The reduction of the corporate tax rate under the TCJA may cause a reduction in the economic benefit of our NOLs and other deferred tax assets available to us. Under current law, NOLs that arose before January 1, 2018, will begin to expire in 2041. NOLs that arose after 2017 may be used to offset at most 80% of our taxable income to the extent not offset by pre-2018 NOLs. As a result, we may become required to pay federal income taxes in future years despite having generated losses for federal income tax purposes in prior years.

Risks Related to the Development of our Product Candidates

Our product candidates are based on our ImmTOR platform, which is an unproven approach designed to induce antigen-specific immune tolerance to biologic drugs. We are very early in most of our clinical development efforts and may not be successful in our efforts to use our ImmTOR platform to build a pipeline of product candidates and develop marketable drugs.

All of our product candidates are derived from our ImmTOR platform, which is an unproven approach to induce antigen-specific immune tolerance and to mitigate the immunogenicity of biologic therapies currently being implemented to treat patients. We are developing our ImmTOR platform to restore self-tolerance to autoantigens and potentially treat autoimmune diseases, to be co-administered with AAV gene therapies to potentially enable redosing of said gene therapies and improve and enable activity in biologics (including therapeutic enzymes and other immunogenic drugs).

While we have completed our early development clinical trials and a Phase 2 clinical trial for SEL-212, we have not completed a clinical trial for any other product candidate, nor have we demonstrated our ability to successfully complete any Phase 3 or other pivotal clinical trials, obtain regulatory approvals, manufacture a commercial product, or arrange for a third party to do so on our behalf, or conduct other sales and marketing activities necessary for successful product commercialization. We may have problems identifying new product candidates and applying our technologies to these other areas. Even if we are successful in identifying new product candidates, they may not be suitable for clinical development, including as a result of harmful side effects, limited efficacy or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. The success of our product candidates will depend on several factors, including the following:

- design, initiation and completion of preclinical studies and clinical trials with positive results;
- reliance on third parties, including but not limited to collaborators, licensees, clinical research organizations and contract manufacturing organizations;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates and not infringing or violating patents or other intellectual property of third parties;
- making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities, or establishing such capabilities ourselves;
- launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients and the medical community;
- effectively competing with other therapies;
- obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for our products, if approved;
- maintaining an acceptable safety profile of our products following approval; and
- maintaining and growing an organization of scientists and business people who can develop and commercialize our product candidates and technology.

The occurrence of any of the foregoing would effectively prevent or delay approval of our lead and other product candidates. The outbreak of COVID-19 may continue to adversely impact our business, including our preclinical studies and clinical trials.

The ongoing COVID-19 pandemic has impacted our business and we expect it to continue to do so. In response to the spread of COVID-19, we closed our principal executive office with our administrative employees continuing their work outside of our office and limited the number of staff in any given research and development laboratory. As COVID-19 continues to spread in the United States and elsewhere, we may experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays or difficulties in enrolling or sustaining patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, such as ImmTOR including interruption in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals and clinics serving as our clinical trial sites and hospital and clinic staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, or the closing of clinical trial sites due to the virus, the occurrence of which could affect the integrity of clinical trial data;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, or will withdraw from the clinical trial due to concerns over COVID-19, which could impact the results of the clinical trial, including by increasing the number of observed adverse events, or reducing the statistical power of the clinical trials;
- interruptions or delays in preclinical studies due to restricted or limited operations at our research and development laboratory facility;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- refusal of the FDA to accept data from clinical trials in affected geographies;
- changes to the clinical endpoints, statistical analysis plan, or enrollment plans for ongoing clinical trials due to limitations in patients, resources, or sites due to COVID-19;
- interruption or delays to our sourced discovery and clinical activities; and
- impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans.

The extent to which the COVID-19 pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

We are applying our ImmTOR platform to antigen-specific immune tolerance for gene therapy involving gene augmentation, replacement or editing. Regulatory authorities in the United States and European Union have limited experience in reviewing and approving gene therapy products, which could affect the time and data required to obtain marketing authorization of any of our product candidates.

Our future success depends in part on our successful development of viable gene therapy product candidates utilizing our ImmTOR platform.

The regulatory approval process for gene therapy product candidates can be more lengthy, rigorous and expensive than the process for other better known or more extensively studied product candidates and technologies. Since we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the European Medicines Agency, or the EMA, or comparable regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. This may be a particularly significant risk for many of the genetically defined diseases for which we may develop

product candidates alone or with collaborators due to small patient populations for those diseases, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing genome editing technology in a timely manner or under technically or commercially feasible conditions. Even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in regulations or the interpretation of regulations by applicable regulatory agencies.

Changes in applicable regulatory guidelines may lengthen the regulatory review process for our product candidates, require additional studies or trials, increase development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of such product candidates, or lead to significant post-approval limitations or restrictions. Additionally, adverse developments in clinical trials conducted by others of gene therapy products or products created using genome editing technology, or adverse public perception of the field of genome editing, may cause the FDA, the EMA and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. Furthermore, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the development or commercialization of current or future product candidates.

Even if we comply with applicable laws, rules, and regulations, and even if we maintain close coordination with the applicable regulatory authorities with oversight over our product candidates, our development programs may fail to succeed. Regulatory authorities have substantial discretion in the approval process and may refuse to accept a marketing application as deficient or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Additionally, adverse developments in clinical trials conducted by others of gene therapy products or products created using genome editing technology, or adverse public perception of the field of genome editing, may cause the FDA and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market would materially and adversely affect our business, financial condition, results of operations and prospects.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Except for SEL-212 and SEL 302, our product candidates are in preclinical development. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval, and the risk of failure through the development process is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Preclinical development is costly and inherently uncertain. Early preclinical results may not be predictive of future results, however, if our technology proves to be ineffective or unsafe as a result of, among other things, adverse side effects, pre-existing anti-drug antibodies that can neutralize the viral vector and block gene transfer, or cellular immune response to the transduced cells, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the clinical development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate for its intended indications. Clinical testing is expensive, difficult to design and implement, can take many years to complete and its outcome is inherently uncertain. A failed clinical trial can occur at any stage of testing. Moreover, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, the topline clinical trial results we reported from our Phase 2 head-to-head COMPARE study of SEL-212 and the top-line data from our SEL-399 program may not be predictive of future results. Moreover, we may not be able to complete, or may be required to deviate from the current clinical trial protocol for a variety of reasons.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in preclinical development or early-stage clinical trials, and we cannot be certain that we will not face similar setbacks. SAEs caused by, or other unexpected properties of, any product candidates that we may choose to develop could cause us, an institutional review board or regulatory authority to interrupt, delay or halt clinical trials of one or more of such product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable non-U.S. regulatory authorities. If any product candidate that we may choose to develop is associated with SAEs or other unexpected properties, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which those undesirable characteristics would be expected to be less prevalent, less severe or more tolerable from a risk-benefit perspective. In the SEL-212 Phase 1/2 clinical program, we have observed multiple SAEs, and future SAEs may occur causing us to incur additional costs or experience delays in completing, or causing us to ultimately be unable to complete, the development and commercialization of our product candidates, and delay or prevent our ability to

obtain FDA approval. Moreover, preclinical and clinical data is often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or other regulatory authority approval. If we fail to produce positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be negatively impacted.

In addition, we cannot be certain as to what type and how many clinical trials the FDA will require us to conduct before we may gain regulatory approval to market any of our product candidates in the United States or other countries, if any. Prior to approving a new therapeutic product, the FDA generally requires that safety and efficacy be demonstrated in two adequate and well-controlled clinical trials.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval for, or commercialize, our product candidates, including:

- clinical trials of our product candidates may produce unfavorable, incomplete or inconclusive results;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or may place a clinical hold on existing clinical trials;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with contract research organizations, or CROs, or clinical trial sites;
- we may be unable to recruit suitable patients to participate in a clinical trial, the number of patients required for clinical trials of our product candidates may be larger than we expect, enrollment in these clinical trials may be slower than we expect or participants may drop out of these clinical trials at a higher rate than we expect, or enrollment could be affected by the ongoing COVID-19 pandemic or the ongoing conflict in Ukraine;
- the number of clinical trial sites required for clinical trials of our product candidates may be larger than we expect;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- investigators, regulators, data safety monitoring boards or institutional review boards may require that we or our investigators suspend or terminate clinical research, or we may decide to do so ourselves;
- investigators may deviate from the trial protocol, fail to conduct the trial in accordance with regulatory requirements or misreport study data;
- the cost of clinical trials of our product candidates may be greater than we expect or we may have insufficient resources to pursue or complete certain aspects of our clinical trial programs or to do so within the timeframe we planned;
- the supply or quality of raw materials or manufactured product candidates (whether provided by us or third parties) or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or in a timely manner, or we may experience interruptions in supply;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we expect;
- the FDA or comparable foreign regulatory authorities may disagree with our clinical trial design or our interpretation of data from preclinical studies and clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design of our clinical trials;
- regarding trials managed by our existing or any future collaborators, our collaborators may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but potentially suboptimal for us; and
- geopolitical events may affect international and overseas trial sites in ways beyond our control.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, or if we are forced to delay or abandon certain clinical trials or other testing in order to conserve capital resources, we may:

- be delayed in obtaining marketing approval for our product candidates, if at all;
- lose the support of collaborators, requiring us to bear more of the burden of research and development;

- obtain marketing approval in some countries and not in others;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have a product removed from the market after obtaining marketing approval.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. We could also encounter delays if a clinical trial is suspended or terminated. Authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

We filed an IND to conduct a Phase 1/2 clinical trial of our SEL-302 product candidate in pediatric patients with methylmalonic acidemia in the third quarter of 2021. On November 23, 2021, this trial was placed on clinical hold by the FDA, with questions specifically relating to CMC of the AAV vector. On February 9, 2022, we submitted a written response to the FDA to answer its questions. On March 9, 2022, we received a letter from the FDA indicating the clinical hold was removed and the trial may proceed. ImmTOR manufacturing continues to proceed in accordance with our expectations, and we have not observed any impact to any of our ImmTOR programs.

Our product development costs will increase if we experience delays in clinical testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In addition, from time to time our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. For example, SEL-212 is being developed for the treatment of chronic refractory gout, which affects a small patient population. Accordingly, there is a limited number of patients who could enroll in our clinical studies for SEL-212. Additionally, the DISSOLVE II trial of SEL-212 has enrolled subjects at clinical sites located in Russia and Ukraine. As a result of the ongoing and rapidly evolving situation in the region, we may remove those patients from the trial, which as a result could potentially result in delays in the full enrollment of the study and/or the release of top-line results. The safety of our patients and investigators continues to be our utmost priority. Additionally, the COVID-19 pandemic has affected our ability to enroll and sustain patients in our clinical trials, and could result in the inability of some patients to complete our clinical trials. Additionally, we have enrolled subjects in countries where patient populations have less or limited access to COVID-19 vaccines, which could result in further delays in enrollment or a patient's inability to complete our clinical trials. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which could cause the value of our common stock to decline and limit our ability to obtain additional financing.

We may conduct clinical trials for product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations or the complexity of regulatory burdens may otherwise adversely impact us.

Opening trial sites outside the United States may involve additional regulatory, administrative and financial burdens, including compliance with foreign and local requirements relating to regulatory submission and clinical trial practices. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practices, or GCPs, and the FDA must be able to validate the data from the trial through an onsite inspection, if necessary. Generally, the patient population for any clinical trials conducted

outside the United States must be representative of the population for which we intend to seek approval in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. Nonetheless, there can be no assurance that the FDA will accept data from trials conducted outside the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay or permanently halt our development of any applicable product candidates.

Additional risks inherent in conducting international clinical trials include:

- foreign regulatory requirements that could burden or limit our ability to conduct our clinical trials;
- increased costs and heightened supply constraints associated with the acquisition of standard of care drugs and/or combination or comparator agents for which we may bear responsibility in certain jurisdictions;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations;
- more burdensome manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- lack of consistency in standard of care from country to country;
- diminished protection of intellectual property in some countries; and
- changes in country or regional regulatory requirements; and
- geopolitical instability or wars in regions outside of the United States where we conduct clinical trials may impact ongoing clinical trials.

We may not be able to qualify for or obtain various designations from regulators that would have the potential to expedite the review process of one or more of our product candidates and even if we do receive one or more such designations there is no guarantee that they will ultimately expedite the process, or aid in our obtaining marketing approval or provide market exclusivity.

There exist several designations that we can apply for from the FDA and other regulators that would provide us with various combinations of the potential for expedited regulatory review, certain financial incentives as well as the potential for post-approval exclusivity for a period of time. These designations include but are not limited to orphan drug designation, breakthrough therapy designation, accelerated approval, fast track status and priority review for our product candidates. For example, we and AskBio received orphan drug designation for SEL-302 in November 2020. We expect to seek one or more of these designations for our current and future product candidates. There can be no assurance that any of our other product candidates will qualify for any of these designations. There can also be no assurance that any of our product candidates that do qualify for these designations will be granted such designations or that the FDA will not revoke a designation it grants at a later date. Further, there can be no assurance that any of our product candidates that are granted such designations will ever benefit from such designations or that the FDA would not withdraw such designations once granted. Were we to receive a designation that promised a period of market exclusivity, such as orphan drug exclusivity, such exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Further with respect to orphan drug status, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care.

Interim, top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, top-line or preliminary data from our clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a full analyses of all data related to the particular trial. For example, we and AskBio announced top-line data from the Phase 1 trial for SEL-399 in November 2021. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Interim, top-line or preliminary data

may not be representative of final data. If final data is not as positive as earlier interim, top-line or preliminary we have released, our business prospects would be significantly harmed.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. As a result, preliminary and top-line data should not be relied upon in making an investment decision in our securities.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or compromise our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target and prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials, could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities and could result in decreased market acceptance of any of our product candidates, if approved. Further, therapies such as those we are developing involve unique side effects that could be more significant than side effects from other types of therapies with singular components. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications.

Further, the clinical development of SEL-212 over many years has required multiple clinical trials and resulted in the use of different formulations of ImmTOR. While we do not believe that such differences in formulation will affect the safety or the efficacy of SEL-212, we cannot guarantee that any such formulation changes will not negatively impact the results of any clinical trials related to SEL-212, or result in a significant difference in the safety and efficacy of SEL-212.

The drug-related side effects observed in our clinical trials could also affect patient enrollment in our clinical trials or the ability of any enrolled patients to complete such trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- regulatory authorities may impose additional restrictions on the marketing of, or the manufacturing processes for, the particular product;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients, or become subject to fines, injunctions or the imposition of civil or criminal penalties;
- our reputation may suffer; and
- we could be required to develop a REMS plan to prevent, monitor and/or manage a specific serious risk by informing, educating and/or reinforcing actions to reduce the frequency and/or severity of the event.

Any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

Risks Related to our Dependence on Third Parties and Manufacturing

We rely on 3SBio in China as our primary supplier of pegadricase and on other third parties for the manufacture of our product candidates for preclinical and clinical testing, and expect to continue to do so for the foreseeable future. Our reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or that such quantities may not be available at an acceptable cost, or in compliance with regulatory requirements, which could delay, prevent or impair our development or commercialization efforts.

We obtain the biologic pegadricase, a component of SEL-212, primarily from 3SBio in China. Under the 3SBio License, we have limited rights to manufacture pegadricase and while we have entered into a contract with a back-up supplier located outside of China, we expect to continue to rely on 3SBio as the primary supplier of pegadricase for the foreseeable future.

Any disruption in production or inability of 3SBio in China to produce adequate quantities of pegadricase to meet our needs could impair our ability to operate our business on a day-to-day basis and to continue our research and development of our future product candidates. Furthermore, since 3SBio is located in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies, laws, rules and regulations of the United States or Chinese governments, political unrest or unstable economic conditions in China. For example, trade tensions between the United States and China have been escalating in recent years. Most notably, several rounds of U.S. tariffs have been placed on Chinese goods being exported to the United States. Each of these U.S. tariff impositions against Chinese exports were followed by a round of retaliatory Chinese tariffs on U.S. exports to China. Pegadricase is subject to, and any other components we purchase from China may be subject to, these tariffs, which could increase our manufacturing costs and could make our products, if successfully developed and approved, less competitive than those of our competitors whose inputs are not subject to these tariffs.

Moreover, as a result of the COVID-19 pandemic, certain of our suppliers and CMOs in the United States, China and other countries may be affected, which could disrupt their activities. We could face difficulty sourcing key components necessary to produce supply of SEL-212, which may negatively affect our clinical development activities and our agreement with Sobi. If COVID-19 continues to impact U.S. business operations, including those of our CMOs and suppliers, we could face additional disruptions to our supply chain that could affect the supply of drug product for our preclinical studies and clinical trials. Additionally, as our CMOs are producers of drug substances and drug products, including vaccines and therapeutics, they could be compelled by a national government, or choose themselves, to shift their resources to the production of a COVID-19 vaccine and/or therapeutics for COVID-19, which could disrupt any scheduled drug substance or drug product batches we may have and may prevent us from obtaining supplies for our programs in a timely manner to meet our development timelines.

Any of these matters could materially and adversely affect our business and results of operations. Any issues related to the manufacturing lots or similar action regarding pegadricase used in preclinical studies or clinical trials could delay the studies or trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply or maintain compliance with regulatory requirements by 3SBio could significantly delay our clinical development of potential products and reduce third-party or clinical researcher interest and support of our proposed trials. These interruptions or failures could also impede commercialization of our future product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currency in China. Future appreciation of the local currency could increase our costs. These factors and increasing wage rates due to increased demand for skilled laborers and the declining availability of skilled labor in China could cause our labor costs to rise.

We rely, and expect to continue to rely, in addition to 3SBio, on other third parties for the manufacture of our product candidates for supply in preclinical studies and clinical trials, as well as for commercial manufacture if any of our product candidates receive marketing approval. Our reliance on such third parties increases the risk that we will not have sufficient quantities of our product candidates on a timely basis or at all, or that such quantities will be available at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. For example, we rely on third parties for the manufacture of our gene therapy preclinical materials. Gene therapy is a relatively new area for commercial biopharmaceutical development and there are a limited number of CMOs with adequate facilities and expertise in this area. As a result, we may be unable to successfully manufacture our gene therapy preclinical materials through a third party or scale up the manufacture of our gene therapy product candidates for clinical testing or commercialization, if at all.

We may be unable to establish any agreements with third-party manufacturers on acceptable terms or at all, and even if we do rely on third-party manufacturers entails additional risks, including the:

- inability, failure or unwillingness of third-party manufacturers to comply with regulatory requirements, maintain quality assurance, meet our needs, specifications or schedules or continue to supply products to us;
- reduced control we have over product development, including with respect to our lead product candidate, due to our reliance on such third-party manufacturers,
- breach of manufacturing agreements by the third-party manufacturers;

- misappropriation or disclosure of our proprietary information, including our trade secrets and know-how;
- relationships that the third-party manufacturer may have with others, some of which may be our competitors, and, if it does not successfully carry out its contractual duties, does not meet expectations, experiences work stoppages, or needs to be replaced, we may need to enter into alternative arrangements, which may not be available, desirable or cost-effective; and
- termination or nonrenewal of agreements by third-party manufacturers at times that are costly or inconvenient for us.

Additionally, if our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. In addition, there are a limited number of manufacturers that operate under cGMP regulations that might be capable of manufacturing our products. Therefore, our product candidates and any future products that we may develop may compete with other products for access to manufacturing facilities. Any failure to gain access to these limited manufacturing facilities could severely impact the clinical development, marketing approval and commercialization of our product candidates.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for required raw materials used in the manufacture of our product candidates or for the manufacture of finished product. Moreover, we often rely on one CMO to produce multiple product components. For instance, one of our CMOs produces several polymers used in our ImmTOR platform. If our current CMOs cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. Our current and expected future dependence upon others for the manufacture of our product candidates or products could delay, prevent or impair our development and commercialization efforts.

If we are unable to maintain any of our existing collaborations, or if these arrangements are not successful, or we are unable to enter into future licenses, our business could be adversely affected.

We have entered into collaborations with other parties, including pharmaceutical and biotechnology companies and universities, to develop products based on our ImmTOR platform, and such collaborations and licensing arrangements currently represent a significant portion of our product pipeline and are expected to represent a larger portion of our pipeline in the future. Certain of our collaborations have provided us with important funding for some of our development programs and we expect to receive additional funding under collaborations in the future although not all of our collaborations may result in funding to us, and certain collaborations, licenses and agreements may result in increased expenditures by us. Our existing collaborations, and any future collaborations, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on preclinical or clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization

of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- collaborations may be terminated and we would potentially lose the right to pursue further development or commercialization of the applicable product candidates as well as have difficulty entering into a similar collaboration where the potential collaborator is aware of the prior termination;
- collaborators may learn about our technology and use this knowledge to compete with us in the future;
- there may be conflicts between different collaborators that could negatively affect those collaborations and potentially others; and
- the number and type of our collaborations could adversely affect our attractiveness to future collaborators or acquirers.

We are actively exploring licenses and other strategic collaborations with additional pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. However, we face significant competition in seeking appropriate collaborators. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may not be able to access specific antigens that would be suitable to development with our technology, have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our programs, and our business may be materially and adversely affected.

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including by failing to meet deadlines for the completion of such trials.

We rely, and expect to continue to rely, on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct and manage our clinical trials, including our ongoing Phase 3 DISSOLVE clinical program for SEL-212, consisting of the DISSOLVE I and DISSOLVE II trials, which we have agreed to continue to run on behalf of Sobi, and for our other product candidates. We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials.

While we rely on these third parties for research and development activities, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCP regulations, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, safety and welfare of trial participants are protected. Other countries' regulatory agencies also have requirements for clinical trials. If we or any of our CROs or third-party contractors fail to comply with applicable GCPs, the data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, *www.ClinicalTrials.gov*, within specified timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, do not comply with confidentiality obligations, do not meet expected deadlines, experience work stoppages, terminate their agreements with us or need to be replaced, or do not conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may need to enter into new arrangements with alternative third parties, which could be difficult, costly or impossible, and our clinical trials may be extended, delayed or terminated, or may need to be repeated. If any of the foregoing occur, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates or in commercializing our product candidates.

We have no experience manufacturing our product candidates for commercial use, and if we decide to establish our own commercial manufacturing facility, we cannot assure you that we can manufacture our product candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable.

We have a pilot manufacturing facility at our Watertown, Massachusetts location where we conduct process development, scale-up activities and the manufacture of ImmTOR product candidates for preclinical use. We do not currently have any of our own manufacturing facilities that meet the FDA's cGMP requirements for the production of any product candidates used in humans, and rely on our CMOs for clinical production. We currently have no plans to establish our own commercial manufacturing facilities and we will continue to rely on our partnership with CMOs who are currently producing ImmTOR at the commercial scale for SEL-212 using our proprietary process and equipment.

Risks Related to Commercialization of our Product Candidates and Legal Compliance Matters

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, safety and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- product labeling or product insert requirements of the FDA or foreign regulatory authorities, including any limitations or warnings contained in a product's approved labeling, including any black box warning or REMS;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- our ability to hire and retain a sales force in the United States;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for our product candidates, once approved;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

We currently have no sales organization and expect to rely on Sobi for the marketing and sale of SEL-212, if approved. If we are unable to establish effective sales, marketing and distribution capabilities, or enter into agreements with third parties with such capabilities, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product candidate for which we obtain marketing approval, we will need to establish a sales and marketing organization or make arrangements with third parties to perform sales and marketing functions and we may not be successful in doing so. We expect to rely on Sobi for the marketing and sale of SEL-212, if approved. For our other product candidates, we expect to build a focused sales and marketing infrastructure to market or co-promote our product candidates in the United States and potentially elsewhere, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

We face substantial competition, including from biosimilars, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The development and commercialization of new drug and biologic products and technologies is highly competitive and is characterized by rapid and substantial technological development and product innovations. We are aware that pharmaceutical and biotechnology companies, offer or are pursuing the development of pharmaceutical products or technologies that may address one or more indications that our product candidates target, as well as smaller, early-stage companies, that offer or are pursuing the development of pharmaceutical products or technologies that may address one or more indications that our product candidates target. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources, established presence in the market and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and reimbursement for product candidates and in marketing approved products than we do.

These third parties compete with us in recruiting and retaining qualified scientific, sales and marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market, especially for any competitor developing a competing immunomodulating therapeutic that will likely share our same regulatory approval requirements. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic or biosimilar products.

We expect the product candidates we develop will be regulated as biological products, or biologics, and therefore they may be subject to competition sooner than anticipated.

The BPCIA was enacted as part of the Affordable Care Act to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an approved biologic. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a BLA. The law is still being interpreted and implemented by the FDA, and as a result, its ultimate impact, implementation, and meaning are subject to uncertainty. However, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any product candidate approved in the United States as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to Congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations or third-party coverage or reimbursement policies, any of which would have a material adverse effect on our business.

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval, especially novel products like our gene therapy product candidates, and may be particularly difficult because of the higher prices associated with gene therapy product candidates. Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

Obtaining and maintaining adequate reimbursement for our products may be difficult. We cannot be certain if we will obtain an adequate level of reimbursement for our products by third-party payors. Even if we do obtain adequate levels of reimbursement, third-party payors, such as government or private healthcare insurers, carefully review and question the coverage of, and challenge the prices charged for, products. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Third-party payors often require that pharmaceutical companies provide them with predetermined discounts from list prices and are challenging the prices charged for products. We may also be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. Some third-party payors may require pre-approval of coverage for new and innovative therapies, such as our product candidates, before they will provide reimbursement. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new products,

if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control, including possible price reductions, even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval. There can be no assurance that our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically necessary for a specific indication or cost-effective, or that coverage or an adequate level of reimbursement will be available.

Moreover, there is heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. There can be no assurance that our product candidates, will not be subject to heightened governmental scrutiny, unfavorable regulatory inquiry or action, or Congressional inquiry.

Product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- loss of clinical trial participants or increased difficulty in enrolling future participants;
- significant costs to defend the related litigation or to reach a settlement;
- substantial payments to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy;
- the inability to commercialize any products that we may develop;
- distraction of management’s attention from our primary business; and
- substantial monetary awards to patients or other claimants;

We maintain general liability, product liability and umbrella liability insurance. Our existing insurance coverage may not fully cover potential liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. A product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the commercialization of any product candidates we develop.

Our relationships with healthcare providers, customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties,

exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Arrangements with physicians, others who may be in a position to generate business for us, and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- the federal False Claims Act, which impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the federal government claims for payment that are false or fraudulent. Private individuals (e.g., whistleblowers) can bring these actions on behalf of the government; in addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- HIPAA which imposes criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- HIPAA, as amended by HITECH and its implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act, which requires applicable manufacturers of certain products for which payment is available under a federal healthcare program to report annually to the government information related to certain payments or other “transfers of value” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022, and teaching hospitals, as well as ownership and investment interests held by the physicians and their immediate family members;
- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by third-party payors, including private insurers; and requirements to comply with federal and pharmaceutical industry compliance guidelines;
- state data privacy and price transparency laws, many of which differ from each other in significant ways and often are broader than and not preempted by HIPAA or the Sunshine Act, thus complicating compliance efforts; by way of example, the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for “protected health information” maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context; and
- similar healthcare laws and regulations in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain protected information, such as the General Data Protection Regulation, or GDPR, which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the European Union (including health data); in addition, the United Kingdom leaving the EU could also lead to further legislative and regulatory changes. It remains unclear how the United Kingdom data protection laws or regulations will develop in the medium to longer term and how data transfer to the United Kingdom from the E.U. will be regulated. However, the United Kingdom has transposed the GDPR into domestic law with the Data Protection Act 2018, which remains in force following the United Kingdom’s departure from the EU

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom may recommend, purchase and/or prescribe our product candidates, if approved, may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or

any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

For example, the ACA, is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. We cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. Separately, in response to the COVID-19 pandemic, the FDA has periodically modified its regular practices with respect to inspection of manufacturing facilities. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can have a material adverse effect on our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations administered by the U.S. Commerce Department's Bureau of Industry and Security, U.S. customs regulations, various economic and trade sanctions regulations including those administered or enforced by relevant government authorities, such as by the U.S. Treasury Department's Office of Foreign Assets Control or the U.S. Department of State, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. U.S. sanctions laws and regulations may govern or restrict our business and activities in certain countries and with certain persons. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors and other partners from authorizing, promising, offering or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our product candidates abroad once we enter a commercialization phase, and/or to obtain necessary

permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Our violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

If we or our contract manufacturers or other third parties fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We and our contract manufacturers and other third parties with whom we do business are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including biological materials and chemicals. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. The failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to our Intellectual Property

If we or our licensors are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would negatively impact our business.

Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner or in all jurisdictions. As we reach the statutory deadlines for deciding whether and where to initiate prosecution in specific foreign jurisdictions by filing national stage applications based on our Patent Cooperation Treaty, or PCT, applications, we will have to decide whether and where to pursue patent protection for the various inventions claimed in our patent portfolio, and we will only have the opportunity to obtain patents in those jurisdictions where we pursue protection. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as, with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business. We also cannot guarantee that any of our patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete and thorough, nor can we be certain that we have identified each and every patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents covering technology that we license from third parties. We may also require the cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, we have obligations under our licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license could have a material adverse impact on our business.

We cannot provide any assurances that the issued patents we currently own, or any future patents, include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. Further, it is possible that a patent claim may provide coverage for some but not all parts of a product candidate or third-party product. These and other factors may provide opportunities for our competitors to design around our patents.

Moreover, other parties may have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications, and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming similar methods or by claiming subject matter that could dominate our patent position. In addition, it may be some time before we understand how the patent office reacts to our patent claims and whether they identify prior art of relevance that we have not already considered.

Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in any owned patents or pending patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we may license patents were the first to make the inventions claimed or were the first to file. For these and other reasons, the issuance, scope, validity, enforceability and commercial value of our patent rights are subject to a level of uncertainty. Our pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates. The issuance, scope, validity, enforceability and commercial value of our patents are subject to a level of uncertainty.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. Due to legal standards relating to patentability, validity, enforceability and claim scope of patents covering biotechnological and pharmaceutical inventions, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Even if issued, a patent's validity, inventorship, ownership or enforceability is not conclusive. Accordingly, rights under any existing patent or any patents we might obtain or license may not cover our product candidates, or may not provide us with sufficient protection for our product candidates to afford a commercial advantage against competitive products or processes, including those from branded and generic pharmaceutical companies.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to assign their inventions to us, and we require all of our employees, consultants, advisors and any other third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary know-how, and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how, and other information and technology. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could adversely affect our business and operations.

Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful. Even if we are successful, domestic or foreign litigation, or USPTO or foreign patent office proceedings, may result in substantial costs and distraction to our management. We may not be able, alone or with our licensors or potential collaborators, to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with

intellectual property litigation or other proceedings, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. In addition, during the course of this kind of litigation or proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be adversely affected.

If we are unable to protect the confidentiality of our trade secrets and know-how, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also seek to enter into confidentiality and invention or patent assignment agreements with our employees, advisors and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Our trade secrets may also be obtained by third parties by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to, or independently developed by, a competitor, our competitive position would be harmed.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, recent patent reform legislation could further increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith Act America Invents Act, or the Leahy-Smith Act, included provisions that affect the way patent applications are prosecuted and may also affect patent litigation, including first-to-file provisions. A third party that files a patent application in the USPTO before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This requires us to be cognizant of the time from invention to filing of a patent application. Thus, for our U.S. patent applications containing a priority claim after March 16, 2013, the date such provisions became effective, there is a greater level of uncertainty in the patent law. Moreover, some of the patent applications in our portfolio will be subject to examination under the pre-Leahy-Smith Act law and regulations, while other patents applications in our portfolio will be subject to examination under the law and regulations, as amended by the Leahy-Smith Act. This introduces additional complexities into the prosecution and management of our portfolio.

In addition, the Leahy-Smith Act limits where a patentee may file a patent infringement suit and provides opportunities for third parties to challenge any issued patent in the USPTO. These provisions apply to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a federal court action.

Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims because it may be easier for them to do so relative to challenging the patent in a federal court action. It is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. From time to time, the U.S. Supreme Court, other federal courts, the U.S. Congress or the USPTO may change the standards of patentability, and any such changes could have a negative impact on our business.

Depending on these and other decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change or be interpreted in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue to us in the future. In addition, these events may adversely affect our ability to defend any patents that may issue in procedures in the USPTO or in courts.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. While no such litigation has been brought against us and we have not been held by any court to have infringed a third party's intellectual property rights, we cannot guarantee that our technology, product candidates or use of our product candidates do not infringe third-party patents.

We are aware of numerous patents and pending applications owned by third parties, and we monitor patents and patent applications in the fields in which we are developing product candidates, both in the United States and elsewhere. However, we may have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference or derivation proceedings before the USPTO and similar bodies in other countries. Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found, or believe there is a risk we may be found, to infringe a third party's intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing and marketing our product candidates and technology. However, we may not be able to obtain any such license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Even if we are successful in such proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. There could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Any of these risks coming to fruition could have a material adverse impact on our business.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, and our issued patents covering our product candidates could be found invalid or unenforceable or could be interpreted narrowly if challenged in court.

Competitors may infringe our intellectual property, including our patents or the patents of our licensors. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. This can be expensive, particularly for a company of our size, and time-consuming. If we initiated legal proceedings against a third party to enforce a patent, if and when issued, covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement, or failure to claim patent-eligible subject matter. Grounds for unenforceability assertions include allegations that someone connected with the prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may

also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings and equivalent proceedings in foreign jurisdictions, such as opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Moreover, even if not found invalid or unenforceable, the claims of our patents could be construed narrowly or in a manner that does not cover the allegedly infringing technology in question. Such a loss of patent protection would have a material adverse impact on our business.

The lives of our patents may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first effective non-provisional filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates, proprietary technologies and their uses are obtained, once the patent life has expired, we may be open to competition. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. If we do not have sufficient patent life to protect our product candidates, proprietary technologies and their uses, our business and results of operations will be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and, in some jurisdictions, during the pendency of a patent application. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have an adverse effect on our business.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are party to multiple license agreements that impose, and we may enter into additional licensing and funding arrangements with third parties that may impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Under our existing licensing agreements, we are obligated to pay royalties on net product sales of product candidates or related technologies to the extent they are covered by the agreement. Our results of operations will be affected by the level of royalty payments that we are required to pay to third parties. We cannot precisely predict the amount, if any, of royalties that we will be required to pay to third parties in the future. Any disagreements with the counterparty over the amount of royalties owed could lead to litigation, which is costly. In addition, if we fail to comply with our obligations under current or future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, or may face other penalties under the agreements. Such an occurrence could materially adversely affect the value of product candidates being developed using rights licensed to us under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. Furthermore, our counterparties may allege that we are operating outside the scope of the licenses granted and terminate our license or otherwise require us to alter development, manufacturing or marketing activities.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to certain intellectual property, through licenses from third parties and under patents and patent applications that we own, to develop our product candidates. Because we may find that our programs require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license compositions, methods of use, processes or other third-party

intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may also engage advisors and consultants who are concurrently employed at universities or other organizations or who perform services for other entities. Although we try to ensure that our employees, advisors and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, advisors or consultants have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such party's former or current employer or in violation of an agreement with another party. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims.

In addition, while it is our policy to require our employees, consultants, advisors and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Similarly, we may be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than in the United States, assuming that rights are obtained in the United States and assuming that rights are pursued outside the United States. In this regard, in addition to the United States, we also seek to protect our intellectual property rights in other countries. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications. For all of the patent families in our portfolio, including the families that may provide coverage for our lead product candidate, the relevant statutory deadlines have not yet expired. Therefore, for each of the patent families that we believe provide coverage for our lead product candidate, we will need to decide whether and where to pursue additional protection outside the United States. In addition, the laws of some foreign countries, do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, for our existing patent rights outside the United States and any foreign patent rights we may decide to pursue in the future, we may not be able to obtain relevant claims and/or we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

If we do not obtain additional protection under the Hatch-Waxman Act and similar foreign legislation extending the terms of our patents for our product candidates, our business may be harmed.

Depending upon the timing, duration and specifics of FDA regulatory approval for our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Patent term restorations, however, are limited to a maximum of five years and cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval by the FDA.

The application for patent term extension is subject to approval by the USPTO, in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension. We may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened, our competitors may obtain earlier approval of competing products and our ability to generate revenues could be materially adversely affected.

Risks Related to our Operations

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Carsten Brunn, Ph.D., our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements or offer letters with Dr. Brunn and other executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing, technology and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We have incurred increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we have incurred and expect to continue to incur significant legal, accounting and other expenses. In particular, beginning with this Annual Report, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. If we are unable to maintain effective internal control over financial reporting, we may not have adequate, accurate or timely financial information, and we may be unable to meet our reporting obligations as a public company or comply with the requirements of the SEC or Section 404. This could result in a restatement of our financial statements, the imposition of sanctions, including the inability of registered broker dealers to make a market in our common stock, or investigation by regulatory authorities. Any such action or other negative results caused by our inability to meet our reporting requirements or comply with legal and regulatory requirements or by disclosure of an accounting, reporting or control issue could adversely affect the trading price of our securities and our business. Material weaknesses in our internal control over financial reporting could also reduce our ability to obtain financing or could increase the cost of any financing we obtain. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

A variety of risks associated with maintaining our subsidiary in Russia or expanding operations internationally could adversely affect our business.

In addition to our U.S. operations, we maintain a wholly owned subsidiary in Russia, Selecta (RUS). However, we plan to wind down these operations. We may face risks associated with maintaining our subsidiary in Russia, or with any international operations, including possible unfavorable regulatory, pricing and reimbursement, legal, political, tax and labor conditions, and risks associated with our compliance with evolving international sanctions, which could harm our business. We may also rely

on collaborators to commercialize any approved product candidates outside of the United States. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting and changing laws and regulations, such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our product candidates in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection of and enforcing our intellectual property rights;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple-payor reimbursement regimes, government payors or patient self-pay systems;
- limits on our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our product candidates and exposure to foreign currency exchange rate fluctuations, which could result in increased operating expenses and reduced revenues;
- natural disasters, political and economic instability, including wars, events of terrorism and political unrest, outbreak of disease, including the COVID-19 pandemic, boycotts, curtailment of trade and other business restrictions, economic sanctions, and economic weakness, including inflation;
- changes in diplomatic and trade relationships;
- challenges in enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- restriction on cross-border investment, including enhanced oversight by the Committee on Foreign Investment in the United States and substantial restrictions on investment from China;
- certain expenses including, among others, expenses for travel, translation and insurance;
- legal risks, including use of the legal system by the government to benefit itself or affiliated entities at our expense, including expropriation of property;
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the FCPA its books and records provisions, or its anti-bribery provisions; and
- risks that we may suffer reputational harm as a result of our operations in Russia.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

Our business and operations would suffer in the event of system failures or unauthorized or inappropriate use of or access to our systems.

Despite the implementation of security measures, our internal computer systems and those of our current and future contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we are not aware of any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

Acquisitions or joint ventures could disrupt our business, cause dilution to our stockholders and otherwise harm our business.

We may acquire other businesses, product candidates or technologies as well as pursue strategic alliances, joint ventures, technology licenses or investments in complementary businesses. We have not made any acquisitions to date, and our ability to do so successfully is unproven. Any of these transactions could be material to our financial condition and operating results and expose us to many risks, including:

- disruption in our relationships with future customers or with current or future distributors or suppliers as a result of such a transaction;

- unexpected liabilities related to acquired companies;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- diversion of management time and focus from operating our business to acquisition integration challenges;
- increases in our expenses and reductions in our cash available for operations and other uses;
- possible write-offs or impairment charges relating to acquired businesses; and
- inability to develop a sales force for any additional product candidates.

Foreign acquisitions involve unique risks in addition to those mentioned above, including those related to integration of operations across different cultures and languages, currency risks and the particular economic, political and regulatory risks associated with specific countries.

Also, the expected benefit of any acquisition may not materialize. Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of future joint ventures or acquisitions, or the effect that any such transactions might have on our operating results.

Risks Related to our Common Stock

The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

The trading price of our common stock is likely to be volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price at which you purchased. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results or progress, or changes in approach or timelines, of clinical trials of our product candidates or those of our competitors;
- failure or discontinuation of any of our development programs;
- commencement of, termination of, or any development related to any collaboration or licensing arrangement;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our collaborators or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- announcement or market expectation of additional financing efforts;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates, projections or development timelines of the investment community or that we provide to the public;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- sale of common stock by us or our stockholders in the future as well as the overall trading volume of our common stock;
- changes in the composition of our stockholder base;

- activity in the options market for shares of our common stock;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

Our executive officers, directors, and principal stockholders, if they choose to act together, will continue to have the ability to control or significantly influence all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock and their respective affiliates, in the aggregate, hold shares representing approximately 31.1% of our outstanding voting stock as of December 31, 2021. As a result, if these stockholders choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors, the composition of our management and approval of any merger, consolidation or sale of all or substantially all of our assets.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock reduce. As of December 31, 2021, we had 123,622,965 shares of common stock outstanding. Also, as of December 31, 2021, 11,039,873 and 394,450 shares of common stock that are subject to outstanding options or restricted stock unit awards, respectively, under our outstanding equity plans are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, and Rule 144 under the Securities Act. Additionally, as of December 31, 2021, up to 10,735,980 shares of common stock are issuable upon exercise of outstanding warrants. If these additional shares of common stock are sold, or it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

We may not have the funds necessary to fulfill our obligation to repurchase certain warrants.

Under certain circumstances, holders of certain warrants issued in December 2019 may require us to repurchase the remaining unexercised portion of such warrants for an amount of cash equal to the value of the warrant as determined in accordance with the Black-Scholes option pricing model and the terms of the warrants. Our ability to repurchase the warrants depends on our ability to generate cash flow in the future. To some extent, this is subject to general economic, financial, competitive, legislative and regulatory factors and other factors that are beyond our control. We cannot be certain that we will maintain sufficient cash reserves or that our business will generate cash flow from operations at levels sufficient to permit us to repurchase the warrants.

Provisions in our restated certificate of incorporation and restated bylaws and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which a stockholder might otherwise receive a premium for its shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Furthermore, our restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders. We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees and agents as it may limit any stockholder’s ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees or agents.

We are involved in two securities class action lawsuits.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. Involvement in such litigation, could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

On August 3, 2020, a stockholder of Selecta filed a stockholder derivative action, purportedly on behalf of Selecta and against certain current and former members of the Company's Board of Directors, as well as one affiliated company owned by a current board member, in the Court of Chancery of the State of Delaware, namely Franchi v. Barabe, et al. The complaint alleges that the individual defendants breached their fiduciary duties and committed corporate waste when they authorized a private placement transaction, announced on December 19, 2019, at a price allegedly below fair value. The complaint further alleges that the four defendant directors who participated in the private placement were unjustly enriched in connection with the transaction. On September 25, 2020, the defendants filed a motion to dismiss the lawsuit. On November 6, 2020, the plaintiff filed an amended complaint, and the defendants filed a second motion to dismiss on January 8, 2021. On December 31, 2020, we received a litigation demand letter from two other putative stockholders relating to the same private placement transaction. On April 12, 2021, the Court of Chancery in the State of Delaware granted a motion to stay the litigation pending a review by a Special Committee appointed by the Company's Board of Directors. While the litigation was stayed, the parties reached an agreement in principle to settle the matter, and they expect to submit documentation to the Court for its approval of the settlement in the near future. We could receive other demands or be subject to other litigation. While we intend to vigorously defend against any demands which we believe to be without merit, there can be no assurance as to the outcome of any stockholder litigation. Unfavorable outcomes in securities class action litigation could require us to pay extensive damages, which could delay or prevent our ability to develop our product candidates and harm our operations.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our corporate headquarters are currently located at 65 Grove Street, Watertown, Massachusetts and consist of 25,078 total square feet of leased office and laboratory space under a lease that expires in May 2028.

We also lease approximately 2,500 square feet of office and laboratory space in Moscow, Russia on a month-to-month basis.

Item 3. Legal Proceedings

On August 3, 2020, a stockholder of Selecta filed a stockholder derivative action, purportedly on behalf of Selecta and against certain current and former members of the Company's Board of Directors, as well as one affiliated company owned by a current board member, in the Court of Chancery of the State of Delaware, namely Franchi v. Barabe, et al. The complaint alleges that the individual defendants breached their fiduciary duties and committed corporate waste when they authorized a private placement transaction, announced on December 19, 2019, at a price allegedly below fair value. The complaint further alleges that the four defendant directors who participated in the private placement were unjustly enriched in connection with the transaction. On September 25, 2020, the defendants filed a motion to dismiss the lawsuit. On November 6, 2020, the plaintiff filed an amended complaint, and the defendants filed a second motion to dismiss on January 8, 2021. On December 31, 2020, we received a litigation demand letter from two other putative stockholders relating to the same private placement transaction. On April 12, 2021, the Court of Chancery in the State of Delaware granted a motion to stay the litigation pending a review by a Special Committee appointed by the Company's Board of Directors. While the litigation was stayed, the parties reached an agreement in principle to settle the matter, and they expect to submit documentation to the Court for its approval of the settlement in the near future.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is publicly traded on The Nasdaq Stock Market under the symbol "SELB."

Holders

As of March 4, 2022, there were approximately 124,288,850 shares of our common stock outstanding held by approximately 30 holders of record. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

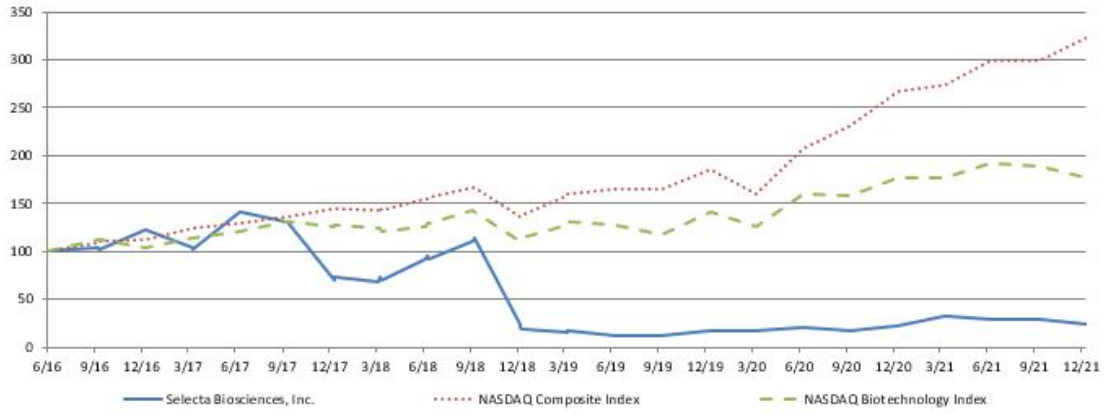
Dividends

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not expect to pay any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments. In addition, our loan and security agreement with Oxford and SVB currently prohibits us from paying dividends on our equity securities, and any future debt agreements may likewise preclude us from paying dividends. See "Management's Discussion and Analysis of Financial Condition and Results of Operations———Liquidity and Capital Resources."

Stock Performance Graph

The graph set forth below compares the cumulative total stockholder return on our common stock between June 21, 2016 (the date of our initial public offering) and December 31, 2021, with the cumulative total return of (a) the Nasdaq Composite Index and (b) the Nasdaq Biotechnology Index, over the same period. This graph assumes the investment of $100 at the market close on June 21, 2016 in our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index and assumes the reinvestment of dividends, if any. The stock price performance of the following graph is not necessarily indicative of future stock price performance.

Comparison Of Cumulative Total Return Selecta Biosciences, Inc.,
NASDAQ COMPOSITE INDEX AND NASDAQ BIOTECHNOLOGY INDEX



This performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities or the Exchange Act.

Purchases of Equity Securities by the Issuer or Affiliated Purchasers

We did not repurchase any of our equity securities during the quarter ended December 31, 2021.

Recent Sales of Unregistered Securities and Use of Proceeds from Registered Securities

None.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Important factors that could cause or contribute to such differences include, but are not limited to, those discussed in Item 1A. "Risk Factors." A discussion of the year ended December 31, 2020 compared to the year ended December 31, 2019 has been reported previously in our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 12, 2021, under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Overview

We are a clinical-stage biopharmaceutical company. Our ImmTOR® platform encapsulates rapamycin, also known as sirolimus, an FDA approved immunomodulator, in biodegradable nanoparticles ImmTOR is designed to induce antigen-specific immune tolerance.

We continually seek to enhance ImmTOR. In recent preclinical studies we have conducted, we have observed that ImmTOR may have synergistic activity with interleukin-2, or IL-2, molecules that have been engineered to be selective for regulatory T cells, or Tregs. Treg-selective IL-2 mutant molecules, or IL-2 muteins, have been shown to transiently expand all pre-existing Tregs in preclinical studies conducted by others. We have observed in preclinical studies that the combination of ImmTOR, a Treg-selective IL-2 mutein and an antigen elicited an approximately three-fold increase in antigen-specific Tregs beyond ImmTOR alone with evidence of enhanced durability of immune tolerance and the potential for ImmTOR dose sparing. This combination of ImmTOR with a Treg selective IL-2 molecule represents an evolution of the ImmTOR platform, which we call ImmTOR-IL™. We believe this combination has the potential to be a best-in-class therapy in diseases where expansion of total Tregs may prove beneficial.

We believe ImmTOR and ImmTOR-IL have the potential to enhance both the efficacy and safety of biologic therapies (including gene therapies), improve product candidates under development, and enable novel therapeutic modalities in autoimmune disease. In clinical trials, ImmTOR has been observed to inhibit the formation of neutralizing antibodies to adeno-associated virus (AAV) capsids, potentially enabling re-dosing of gene therapies. Additionally, based on preclinical data in AAV gene therapies, we believe that ImmTOR has the potential to improve efficacy and safety by increasing transgene expression, reducing hepatic inflammation and inhibiting undesired immune responses to both the AAV capsid and the transgene product that can occur with the first dose of gene therapy. In biologic therapies, clinical activity of ImmTOR in humans has been observed with pegadricase, a highly immunogenic pegylated uricase enzyme being developed for the treatment of patients with chronic refractory gout to conventional therapy. The combination of ImmTOR and pegadricase is currently being evaluated in a Phase 3 clinical trial that we are conducting on behalf of our partner Swedish Orphan Biovitrum AB, or Sobi. We intend to pursue development of therapies for autoimmune diseases where expansion of either all Tregs or antigen-specific Tregs has been shown to, or we believe is, likely to have a beneficial effect. We believe that ImmTOR and ImmTOR-IL have the potential to unlock antigen-specific therapies for autoimmune diseases and that ImmTOR-IL can further improve the efficacy and safety profile of biologic therapies beyond ImmTOR alone.

Impact of COVID-19

We are closely monitoring how the COVID-19 pandemic is affecting our employees, business, preclinical studies and clinical trials. In response to the spread of COVID-19, we have continued to have our administrative employees work outside of our offices and limited the number of staff in any given research and development laboratory. Disruptions caused by the COVID-19 pandemic may result in difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials, and the incurrence of unforeseen costs as a result of preclinical study or clinical trial delays.

While the COVID-19 pandemic has not had a material impact on our clinical programs as of the date of this Annual Report, it could have an impact on our ability to complete the Phase 3 DISSOLVE clinical program of SEL-212, as the pandemic presents the potential to experience delays in enrollment as well as the inability of certain patients to complete the trial due to suffering from COVID-19, our ability to commence preclinical studies and clinical trials of our IgA nephropathy, gene therapy, and autoimmune disease programs, and our ability to obtain supply of both active drug substances and finished drug product as well as efficient execution of the overall supply chain for SEL-212 and our other programs.

At this time, any impact of COVID-19 on our business, revenues, results of operations and financial condition will largely depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the emergence of new virus variants, travel restrictions and social distancing in the United States and other countries, business closures or disruptions, supply chain disruptions, the ultimate impact on financial markets and the global economy, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Financial Operations

To date, we have financed our operations primarily through public offerings and private placements of our securities, funding received from research grants, collaboration and license arrangements and our credit facility. We do not have any products approved for sale and have not generated any product sales.

Since inception, we have incurred significant operating losses. We incurred net losses of $25.7 million and $68.9 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $430.3 million. We expect to continue to incur significant expenses and operating losses for at least the next several years as we:

- continue the research and development of our other product candidates as well as product candidates that we may be developing jointly with collaboration partners;
- seek to enhance our ImmTOR platform and discover and develop additional product candidates;
- seek to enter into collaboration, licensing and other agreements, including, but not limited to research and development, and/or commercialization agreements;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- potentially establish a sales, marketing and distribution infrastructure and scales-up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio, including through licensing arrangements; and
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our operations as a public company.

Until we can generate substantial product revenues, if ever, we expect to finance our cash needs through a combination of equity offerings, debt financings, and license and collaboration agreements. We may be unable to raise capital when needed or on reasonable terms, if at all, which would force us to delay, limit, reduce or terminate our product development or future commercialization efforts. We will need to generate significant revenues to achieve profitability, and we may never do so.

We believe that our existing cash, cash equivalents, restricted cash, and marketable securities as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2023. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

The consolidated financial information presented below includes the accounts of Selecta Biosciences, Inc. and our wholly owned subsidiaries, Selecta (RUS) LLC, a Russian limited liability company, or Selecta (RUS), and Selecta Biosciences Security Corporation, a Massachusetts securities corporation. All intercompany accounts and transactions have been eliminated.

Collaboration and license revenue

To date, we have not generated any revenue from product sales. Our revenue consists primarily of collaboration and license revenue, which includes amounts recognized related to upfront and milestone payments for research and development funding under collaboration and license agreements. We expect that any revenue we generate will fluctuate from quarter to quarter because of the timing and amounts of fees, research and development reimbursements and other payments from collaborators. We do not expect to generate revenue from product sales for at least the next several years. If we or our collaborators fail to complete the development of our product candidates in a timely manner or fail to obtain regulatory approval as needed, our ability to generate future revenue will be harmed, and will affect the results of our operations and financial position. For a further description of the agreements underlying our collaboration and license revenue, see Notes 2 and 12 to our consolidated financial statements included elsewhere in this Annual Report.

Research and development

Our research and development expenses consist of external research and development costs, which we track on a program-by-program basis and primarily include CMO-related costs, fees paid to CROs and internal research and development costs, which are primarily compensation expenses for our research and development employees, lab supplies, analytical testing, allocated overhead costs and other related expenses. Our internal research and development costs are often devoted to expanding our programs and are not necessarily allocable to a specific target.

We have incurred a total of $364.0 million in research and development expenses from inception through December 31, 2021, with a majority of the expenses being spent on the development of SEL-212 and the remainder being spent on our various discovery and preclinical stage product candidate programs and the general expansion of our technology.

We expense research and development costs as incurred. Conducting a significant amount of research and development is central to our business model. Product candidates in clinical development generally have higher development costs than those in earlier stages of development, primarily due to the size, duration and cost of clinical trials. The successful development of our clinical and preclinical product candidates is highly uncertain. Clinical development timelines, the probability of success and development costs can differ materially from our expectations. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those which we currently expect will be required for the completion of clinical development of a product candidate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time to complete any clinical development.

The following table sets forth the components of our research and development expenses during the periods indicated (in thousands):

	Year Ended December 31,		
	2021	2020	2019
SEL-212	$ 31,446	$ 32,288	$ 25,489
AskBio collaboration	3,888	2,807	—
Preclinical stage product candidate programs	11,080	1,717	1,660
Other internal research and development expenses	22,322	17,693	15,594
Total research and development expenses	$ 68,736	$ 54,505	$ 42,743

In June 2020, we and Sobi entered into the Sobi License. Pursuant to the Sobi License, clinical trial costs incurred to complete development of SEL-212, including but not limited to costs incurred while conducting and completing the Phase 3 DISSOLVE trials, will be reimbursed by Sobi. These costs, when reimbursed, will be recognized as revenue consistent with the revenue recognition methodology disclosed in Note 12 to our consolidated financial statements included elsewhere in this Annual Report. The reimbursable costs exclude any costs of additional development activities required that are related to ImmTOR and that are unrelated to SEL-212.

General and administrative

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, business development and support functions. Other general and administrative expenses include facility-related costs not otherwise allocated to research and development expenses, travel expenses for our general and administrative personnel and professional fees for auditing, tax and corporate legal services, including intellectual property-related legal services.

Investment income

Investment income consists primarily of interest income earned on our cash, cash equivalents and marketable securities.

Interest expense

Interest expense consists of interest expense on amounts borrowed under our credit facilities.

Other income (expense)

Other income was de minimis during the years ended December 31, 2021 and 2020, and for the year ended December 31, 2019 it consists primarily of issuance fees associated with warrant liabilities.

Change in fair value of warrant liabilities

Common warrants classified as liabilities are remeasured at fair value, utilizing a Black-Scholes valuation methodology, quarterly with the change in fair value recognized as a component of earnings.

Foreign currency transaction gain (loss)

The functional currency of our Russian subsidiary is the Russian ruble. In addition to holding cash denominated in Russian rubles, our Russian bank accounts also hold cash balances denominated in U.S. dollars to facilitate payments to be settled in U.S. dollars or other currencies. As of December 31, 2021 and 2020, we maintained cash of $0.3 million in Russian banks, all of which was denominated in U.S. dollars. The amounts denominated in U.S. dollars and used in transacting the day-to-day operations of our Russian subsidiary are subject to transaction gains and losses, which are reported as incurred.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

Collaboration and license revenue

The following is a comparison of collaboration and license revenue for the years ended December 31, 2021 and 2020 (in thousands, except percentages):

	Year Ended December 31,		Increase (decrease)	
	2021	2020		
Collaboration and license revenue	$ 85,077	$ 16,597	$ 68,480	413 %

During the years ended December 31, 2021 and 2020, we recognized $83.5 million and $16.6 million, respectively, under the license agreement with Sobi resulting from both the shipment of clinical supply and the reimbursement of costs incurred for the Phase 3 DISSOLVE clinical program. The significant revenue increase is the result of the continued enrollment of the Phase 3 DISSOLVE clinical program that was initiated in the third quarter of 2020. Additionally, during the year ended December 31, 2021, we recognized $1.0 million under the license agreement with Takeda, $0.4 million for shipments under the license agreement with Sarepta, and $0.1 million resulting from the expiration of the contractual audit term under the Skolkovo Foundation grant.

Research and development

The following is a comparison of research and development expenses for the years ended December 31, 2021 and 2020 (in thousands, except percentages):

	Year Ended December 31,		Increase (decrease)	
	2021	2020		
SEL-212	$ 31,446	$ 32,288	$ (842)	(3)%
AskBio collaboration	3,888	2,807	1,081	39 %
Preclinical stage product candidate programs	11,080	1,717	9,363	545 %
Other internal research and development expenses	22,322	17,693	4,629	26 %
Total research and development expenses	$ 68,736	$ 54,505	$ 14,231	26 %

During the year ended December 31, 2021, our research and development expenses increased by $14.2 million, or 26%, as compared to 2020. The increase in cost was primarily the result of expenses incurred for the preclinical programs, salaries for increases in headcount and AskBio collaboration costs. Additionally, we paid Genovis and Ginkgo, $4.0 million and $0.5 million, respectively, for in-license agreements.

General and administrative

The following is a comparison of general and administrative expenses for the years ended December 31, 2021 and 2020 (in thousands, except percentages):

	Year Ended December 31,		Increase (decrease)	
	2021	2020		
General and administrative	$ 20,938	$ 18,913	$ 2,025	11 %

During the year ended December 31, 2021, our general and administrative expenses increased by $2.0 million, or 11%, as compared to 2020. The increase in costs was primarily the result of stock compensation and consulting fees, offset primarily by reduction in professional fees.

Investment income

Investment income was de minimis for the years ended December 31, 2021 and 2020, respectively.

Loss on extinguishment of debt

For the year ended December 31, 2020, we recognized a $0.5 million loss on extinguishment of the 2017 Term Loan (see Note 9).

Foreign currency transaction gain (loss)

We recognized de minimis foreign currency gains during each of the years ended December 31, 2021 and 2020.

Interest expense

Interest expense was $2.8 million and $1.6 million for the years ended December 31, 2021 and 2020, respectively, representing interest expense and amortization of the carrying costs of our credit facilities.

Change in fair value of warrant liabilities

For the year ended December 31, 2021, we recognized $2.3 million of loss from the change in the fair value of warrant liabilities utilizing the Black-Scholes valuation methodology. The increase in value was primarily driven by a slight increase in the Company's share price, offset by the decrease of outstanding warrants. For the year ended December 31, 2020, we recognized $10.4 million change for the increase in the fair value of warrant liabilities primarily driven by an increase in the share price and volatility.

Other income (expense)

Other income (expense) was de minimis for each of the years ended December 31, 2021 and 2020.

Income taxes

For the year ended December 31, 2021, we recognized $16.0 million of expense for the income taxes primarily related to the license agreement with Sobi upon the Company's election to opt out of the installment sale method of taxation. As a result of this election, the Company has prepaid all taxes related to future Sobi License revenue streams.

Net loss

Net loss for the year ended December 31, 2021 decreased to $25.7 million as compared to a net loss of $68.9 million in 2020 primarily due to increased revenue of $66.9 million under the license agreement with Sobi resulting from both the shipment of clinical supply and the reimbursement of costs incurred for the Phase 3 DISSOLVE clinical program, partially offset by increased research and development expenses on preclinical programs.

Liquidity and Capital Resources

Since our inception, we have incurred recurring net losses. We expect that we will continue to incur losses and that such losses will increase for the foreseeable future. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through a combination of equity offerings, debt financings, third-party funding and other collaborations and strategic alliances.

From our inception through December 31, 2021, we have raised an aggregate of $637.5 million to fund our operations, which includes $118.5 million from the sale of preferred stock, $11.1 million in government grant funding, $36.7 million from borrowings under our credit facilities past and present, $202.4 million from our collaborations and license agreements, $64.5 million in combined net proceeds from our initial public offering, $149.3 million in combined net proceeds from private placements and follow-on offerings of our common stock, and, through December 31, 2021, $55.0 million in aggregate net proceeds from "at-the-market" offerings of our common stock.

As of December 31, 2021, our cash, cash equivalents, restricted cash, and marketable securities were $129.4 million, of which $1.4 million was restricted cash related to lease commitments and $0.3 million was held by our Russian subsidiary designated solely for use in its operations. Our Russian subsidiary cash is consolidated for financial reporting purposes.

In addition to our existing cash equivalents, we receive research and development funding pursuant to our collaboration and license agreements. Currently, funding from payments under our collaboration and license agreements represent our only source of committed external funds.

Collaboration and License Agreements

In-licenses

In October 2021, we entered into the Ginkgo Agreement, and paid Ginkgo a $0.5 million one-time upfront payment and we entered into the Genovis Agreement, and paid Genovis a $4.0 million one-time upfront payment.

On September 7, 2021, we entered into the Cyrus Agreement, and purchased 2,326,934 shares of Cyrus' Series B Preferred Stock, par value $0.0001 per share at a purchase price of $0.8595 per share for $2.0 million.

Out-licenses

On October 1, 2021, we entered into the Takeda Agreement. We received a $3.0 million upfront payment and are entitled to receive up to $1.124 billion in future additional payments over the course of the partnership that are contingent on the achievement of development or commercial milestones or Takeda's election to continue its activities at specified development stages.

In June 2020, we entered into the Sobi License. Sobi paid us a one-time, upfront payment of $75 million, and upon the closing of the Sobi Private Placement, we received an additional $25 million from Sobi in consideration for Sobi's purchase of our common stock at $4.6156 per share. We are eligible to receive $630 million in milestone payments upon the achievement of various development and regulatory milestones and sales thresholds for annual net sales of SEL-212, and tiered royalty payments ranging from the low double digits on the lowest sales tier to the high teens on the highest sales tier. Sobi has agreed to fund the Phase 3 clinical program of SEL-212, which commenced in September 2020. We expect this to substantially reduce our annual operating expenses. Additionally, in June 2020, we entered into the Sarepta Agreement. Sarepta paid us a $2.0 million upfront payment upon closing, and a $3.0 million for the achievement of certain pre-clinical milestones in June 2021.

In December 2019, we entered into the AskBio License Agreement. Pursuant to the AskBio License Agreement, AskBio has exercised its option to exclusively license intellectual property rights covering ImmTOR to research, develop, and commercialize certain AAV gene therapy products utilizing ImmTOR, and targeting the GAA gene, or derivatives thereof, to treat Pompe Disease. We received $7.0 million of upfront fees pursuant to the AskBio License Agreement and are eligible to receive $237 million in milestone payments, and royalties on net sales ranging from the mid-to-high single digits.

Financings

In August 2017, we entered into a sales agreement, or the 2017 Sales Agreement, with Jefferies LLC, as sales agent, to sell shares of our common stock with an aggregate value of up to $50.0 million in an "at-the-market" offering. In August 2020, concurrent with the filing of a new shelf registration statement, we entered into a new sales agreement, or the 2020 Sales Agreement, with Jefferies LLC, as sales agent, pursuant to which we may, from time to time, issue and sell common stock with an aggregate value of up to $50.0 million in an "at-the-market" offering. The 2017 Sales Agreement terminated pursuant to its terms in August 2020. On October 8, 2021, we delivered notice to Jefferies LLC that we were terminating the 2020 Sales Agreement, with effect as of October 19, 2021.

On October 25, 2021, we entered into a Sales Agreement, or the 2021 Sales Agreement, with SVB Leerink LLC to sell shares of our common stock, from time to time, through an "at the market" equity offering program under which SVB Leerink will act as sales agent. The shares of common stock sold pursuant to the 2021 Sales Agreement will be issued pursuant to our shelf registration statement on Form S-3 (File No. 333-241692), filed on August 6, 2020 with the Securities and Exchange Commission and related prospectus supplement, filed on October 25, 2021 with the Securities and Exchange Commission, for aggregate gross sales proceeds of up to $75.0 million.

During the year ended December 31, 2021, we sold 13,767,511 shares of our common stock pursuant to the 2021 and 2020 Sales Agreements, as applicable, for aggregate net proceeds of $51.9 million, after deducting commissions and other transaction costs. During the year ended December 31, 2020, we sold 1,069,486 shares of our common stock pursuant to the 2020 and 2017 Sales Agreements, as applicable, for aggregate net proceeds of $2.1 million, after deducting commissions and other transaction costs.

Indebtedness

On August 31, 2020, we entered into a term loan of up to $35.0 million, consisting of term loans in an aggregate amount of $25.0 million, or the Term A Loan, and term loans in an aggregate amount of $10.0 million, or the Term B Loan, governed by a loan and security agreement among us and Oxford Finance LLC, or Oxford, as collateral agent and a lender, and Silicon Valley Bank, or SVB, as a lender. The Term A Loan was funded in full on August 31, 2020, the proceeds of which were used to repay our previously existing 2017 Term Loan and for general corporate and working capital purposes. The second draw period expired on September 30, 2021 and the Term B Loan is no longer available to be drawn in the future.

The 2020 Term Loan is secured by a lien on substantially all of our assets, other than intellectual property, provided that such lien on substantially all assets includes any rights to payments and proceeds from the sale, licensing or disposition of intellectual property. We also granted Oxford a negative pledge with respect to our intellectual property.

The 2020 Term Loan contains customary covenants and representations, including but not limited to financial reporting obligations and limitations on dividends, indebtedness, collateral, investments, distributions, transfers, mergers or acquisitions, taxes, corporate changes, deposit accounts, and subsidiaries. The 2020 Term Loan also contains other customary provisions, such as expense reimbursement, non-disclosure obligations as well as indemnification rights.

The events of default under the 2020 Term Loan include, but are not limited to, our failure to make any payments of principal or interest under the 2020 Term Loan or other transaction documents, our breach or default in the performance of any covenant under the 2020 Term Loan or other transaction documents, the occurrence of a material adverse event, making a false or misleading representation or warranty in any material respect under the 2020 Term Loan, our insolvency or bankruptcy, any attachment or judgment on our assets of at least approximately $0.5 million, or the occurrence of any default under any of our

agreements or obligations involving indebtedness in excess of approximately $0.5 million. If an event of default occurs, Oxford and SVB are entitled to take enforcement action, including acceleration of amounts due under the 2020 Term Loan. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

For a further description of the 2020 Term Loan, see Note 9 to our consolidated financial statements included elsewhere in this Annual Report.

Future funding requirements

As of the date of this Annual Report, we have not generated any revenue from product sales. We do not know when, or if, we will generate revenue from product sales. We will not generate significant revenue from product sales unless and until we obtain regulatory approval and commercialize one of our current or future product candidates. Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research and development services, laboratory and related supplies, clinical costs, legal and other regulatory expenses, and general overhead costs. We expect that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We are subject to risks in the development of our products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We expect that we will need substantial additional funding to support our continuing operations.

As of December 31, 2021, we had an accumulated deficit of $430.3 million. We anticipate operating losses to continue for the foreseeable future due to, among other things, costs related to research, development of our product candidates, conducting preclinical studies and clinical trials, and our administrative organization. We will require substantial additional financing to fund our operations and to continue to execute our strategy, and we will pursue a range of options to secure additional capital.

We are continually evaluating various potential sources of additional funding such as strategic collaborations, license agreements and the issuance of equity to fund our operations. If we raise additional funds through strategic collaborations and alliances, which may include existing collaboration partners, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. To the extent that we raise additional capital through the sale of equity, the ownership interest of our existing shareholders will be diluted, and other preferences may be necessary that adversely affect the rights of existing shareholders.

We believe that our existing cash, cash equivalents, restricted cash, and marketable securities as of December 31, 2021 will enable us to fund our current planned operations into the third quarter of 2023, though we may realize additional cash resources upon the achievement of certain contingent collaboration milestones or it may pursue additional cash resources through public or private equity or debt financings or by establishing collaborations with other companies. Management's expectations with respect to our ability to fund current and long-term planned operations are based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, we may need to seek additional strategic or financing opportunities sooner than would otherwise be expected. However, there is no guarantee that any collaboration milestones will be achieved or that any of these strategic or financing opportunities will be executed on favorable terms, and some could be dilutive to existing stockholders. If we are unable to obtain additional funding on a timely basis, we may be forced to significantly curtail, delay, or discontinue one or more of its planned research or development programs or be unable to expand our operations, meet long-term obligations or otherwise capitalize on our commercialization of our product candidates.

Additionally, while the potential economic impact brought by and the duration of the COVID-19 pandemic may be difficult to assess or predict, the widespread pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, reducing our ability to access capital as and when needed. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- the number of product candidates that we pursue;
- our collaboration agreements remaining in effect, our entering into additional collaboration agreements and our ability to achieve milestones under these agreements;
- the cost of manufacturing clinical supplies of our product candidates;
- our headcount growth and associated costs;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;

- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates.

Summary of Cash Flows

thousands)	Year Ended December 31, 2021	2020	2019
h (used in) and provided by:			
Operating activities	$ (60,382)	$ 34,881	(51,435)
Investing activities	(17,140)	(741)	229
Financing activities	52,897	14,431	105,041
ect of exchange rate changes on cash	(3)	(58)	34
change in cash, cash equivalents, and restricted cash	$ (24,628)	$ 48,513	53,869

Operating activities

Net cash used in operating activities for the year ended December 31, 2021 was $60.4 million compared to $34.9 million provided in the same period in 2020. The decrease in net cash used in operating activities was primarily due to $12.2 million of net losses, adjusted for non-cash items, and uses of cash of approximately $48.2 million for changes in operating assets and liabilities.

Investing activities

Net cash used in investing activities for the year ended December 31, 2021 was $17.1 million compared to net cash used in investing activities of $0.7 million in the same period in 2020. The net cash used in investing activities in 2021 was primarily to purchase marketable securities and to invest in Cyrus Biotechnology, offset by proceeds from the maturities of marketable securities. The net cash used in investing activities in 2020 was to purchase property and equipment.

Financing activities

Net cash provided by financing activities for the year ended December 31, 2021 was $52.9 million compared to net cash provided by financing activities of $14.4 million in the same period in 2020. The net cash provided by financing activities in 2021 was primarily the result of net proceeds from "at-the-market" offerings and from the exercise of stock options.

The net cash provided by financing activities in 2020 was the result of $10.3 million from the Sobi Private Placement, $24.7 million from the Term A Loan, $2.1 million net proceeds from sales of common stock in "at-the-market" offerings, and $1.0 million proceeds from warrant exercises, offset by $4.4 million of issuance costs paid for December 2019 financing and $19.3 million principal payment on outstanding debt.

Research and development contract obligations

Under our license agreement with MIT, milestone payments are due upon the occurrence of certain events and royalty payments commence upon our commercialization of a product. As of December 31, 2021, contractual obligations were $0.4 million. We have assumed license payments are fully offset by royalty payments in 2028.

Recent Accounting Pronouncements

For a discussion of recently adopted or issued accounting pronouncements please see Note 2 to our consolidated financial statements included elsewhere in this Annual Report.

Off-Balance Sheet Arrangements

As of December 31, 2021, we did not have any off-balance sheet arrangements as defined in the rules and regulations of the Securities and Exchange Commission.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgements that affect the reported amounts of assets, liabilities, revenues and expenses, and disclosure of contingent assets and liabilities in our consolidated financial statements. Actual results may differ from these estimates under different assumptions or conditions and could have a material impact on our reported results. While our significant accounting policies are more fully described in the Notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be the most critical in understanding the judgments and estimates we use in preparing our consolidated financial statements:

Revenue Recognition

Revenue is recognized when a customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. Pursuant to ASC Topic 606, *Revenue from Contracts with Customers (ASC 606)*, a customer is a party that has contracted with an entity to obtain goods or services that are an output of the entity's ordinary activities in exchange for consideration. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract, including whether they are distinct in the context of the contract; (iii) determine the transaction price, including the constraint on variable consideration; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy each performance obligation. We only apply the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations, and assess whether each promised good or service is distinct. If a promised good or service is not distinct, it is combined with other performance obligations. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For example, certain performance obligations associated with Swedish Orphan Biovitrum, or Sobi, Asklepios Biopharmaceutical, Inc., or AskBio, Sarepta Therapeutics, Inc., or Sarepta, and Takeda Pharmaceuticals USA, Inc., or Takeda, (see Note 12) will be satisfied over time, and revenue will be recognized using the output method, based on the proportion of actual deliveries to the total expected deliveries over the initial term.

Collaboration and License Revenue: We currently generate revenue through collaboration and license agreements with strategic collaborators for the development and commercialization of product candidates. Collaboration and license agreements with customers are generally accounted for in accordance with ASC 606. We analyze collaboration arrangements by first assessing whether they are within the scope of ASC Topic 808, *Collaborative Arrangements (ASC 808*), and evaluate whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards that are dependent on the commercial success of such activities. Collaboration agreements with customers that are not within the scope of ASC 808 are accounted for in accordance with ASC 606. To the extent the collaboration agreement is within the scope of ASC 808, we also assess whether any aspects of the agreement are within the scope of other accounting literature (specifically ASC 606). If we conclude that some or all aspects of the agreement are distinct and represent a transaction with a customer, we account for those aspects of the arrangement within the scope of ASC 606. We recognize the shared costs incurred that are not within the scope of other accounting literature as a component of the related expense in the period incurred by analogy to ASC Topic 730, *Research and Development (ASC 730)*, and record reimbursements from counterparties as an offset to the related costs. In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under the agreements in accordance with ASC 606, we perform the five steps above. As part of the accounting for the arrangement, we must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. We use key assumptions to determine the stand-alone selling price, which may include market conditions, reimbursement rates for personnel costs, development timelines and probabilities of regulatory success. The assumptions used to determine the stand-alone selling price and our satisfaction of performance obligations have a material effect on our collaboration and license revenue and may prove to be wrong.

The terms of our arrangements typically include one or more of the following: (i) upfront fees; (ii) milestone payments related to the achievement of development, regulatory, or commercial goals; (iii) royalties on net sales of licensed products; (iv) reimbursements or cost-sharing of research and development (R&D) expenses; and (v) profit/loss sharing arising from co-promotion arrangements.

Licenses of Intellectual Property: If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. If not distinct, the license is combined with other performance obligations in the contract. For licenses that are combined with other performance obligations, we assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring

progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. Optional licenses are evaluated to determine if they are issued at a discount, and therefore, represent material rights and should be accounted for as separate performance obligations.

Milestone Payments: At the inception of each arrangement that includes developmental and regulatory milestone payments, we evaluate whether the achievement of each milestone specifically relates to our efforts to satisfy a performance obligation or transfer a distinct good or service within a performance obligation. If the achievement of a milestone is considered a direct result of our efforts to satisfy a performance obligation or transfer a distinct good or service and the receipt of the payment is based upon the achievement of the milestone, the associated milestone value is allocated to that distinct good or service. If the milestone payment is not specifically related to our efforts to satisfy a performance obligation or transfer a distinct good or service, the amount is allocated to all performance obligations using the relative standalone selling price method. We also evaluate the milestone to determine whether they are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price to be allocated, otherwise, such amounts are constrained and excluded from the transaction price. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the transaction price. Any such adjustments to the transaction price are allocated to the performance obligations on the same basis as at contract inception. Amounts allocated to a satisfied performance obligation shall be recognized as revenue, or as a reduction of revenue, in the period in which the transaction price changes.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the customer's discretion are evaluated to determine if they are distinct and optional. For optional services that are distinct, we assess if they are priced at a discount, and therefore, provide a material right to the licensee to be accounted for as separate performance obligations.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied) in accordance with the royalty recognition constraint.

Clinical Trial Costs

Clinical trial expenses are a significant component of research and development expenses, and we outsource a significant portion of these costs to third parties. Third party clinical trial expenses include patient costs, clinical research organization costs and costs for data management. The accrual for site and patient costs includes inputs such as estimates of patient enrollment, patient cycles incurred, clinical site activations, and other pass-through costs. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheets as a prepaid asset or accrued clinical trial cost. These third party agreements are generally cancellable, and related costs are recorded as research and development expenses as incurred. Non-refundable advance clinical payments for goods or services that will be used or rendered for future R&D activities are recorded as a prepaid asset and recognized as expense as the related goods are delivered or the related services are performed. We also record accruals for estimated ongoing clinical research and development costs. When evaluating the adequacy of the accrued liabilities, we analyze progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by us materially affecting our results of operations. The historical clinical accrual estimates made by us have not been materially different from the actual costs.

Warrant Liabilities

In December 2019, we issued common warrants in connection with a securities purchase agreement between us and a group of institutional investors and certain members of our board of directors. Pursuant to the terms of these common warrants, we could be required to settle the common warrants in cash in the event of certain acquisitions of us and, as a result, the common warrants are required to be measured at fair value and reported as a liability on the balance sheet. We recorded the fair value of the common warrants of $40.7 million upon issuance using the Black-Scholes valuation model, and are required to revalue the common warrants at each reporting date with any changes in fair value recorded on our statement of operations. Inputs used to determine estimated fair value of the common warrant liabilities include the estimated fair value of the underlying stock at the valuation date, the estimated term of the warrants, risk-free interest rates, expected dividends and the expected volatility of the underlying stock. The estimates used to determine the fair value of these common warrants represent our best estimates, but may prove to be wrong. Therefore, the change in fair value of warrant liabilities could be materially different in the future.

Stock-Based Compensation

We account for all stock-based compensation granted to employees and non-employees using a fair value method. Stock-based compensation is measured at the grant date fair value and is recognized over the requisite service period of the awards, usually the vesting period, on a straight-line basis, net of estimated forfeitures. To the extent that actual forfeitures differ from our estimates, the differences are recorded as a cumulative adjustment in the period the estimates were adjusted. Stock-based compensation expense recognized in the consolidated financial statements is based on awards that ultimately vest.

The assumptions used in determining the fair value of stock-based awards represent our best estimates, but the estimates involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different in the future.

Smaller Reporting Company

We qualify as a "smaller reporting company" under the rules of the Securities Act and the Exchange Act. As a result, we may choose to take advantage of certain scaled disclosure requirements available specifically to smaller reporting companies. We will remain a smaller reporting company until the last day of the fiscal year in which the aggregate market value of our common stock held by non-affiliated persons and entities, or our public float, is more than $700 million as of the last business day of our most recently completed second fiscal quarter, or the last day of the fiscal year in which we have at least $100 million in revenue and at least $250 million in public float as of the last business day of our most recently completed second fiscal quarter.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of December 31, 2021 and 2020, we had cash, cash equivalents, restricted cash and marketable securities of $129.4 million and $140.1 million, respectively, consisting of non-interest and interest-bearing money market accounts. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term and the low risk profile of our money market accounts and marketable securities, and our current plan to hold marketable securities to maturity, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents or short-term marketable securities.

Item 8. Financial Statements and Supplementary Data

The consolidated financial statements together with the report of our independent registered public company accounting firm, required to be filed pursuant to this Item 8 are appended to this Annual Report. An index of those consolidated financial statements is found in Item 15.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2021.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act.

Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Based on this assessment, our management concluded that, as of December 31, 2021, our internal control over financial reporting was effective.

Inherent Limitations of Internal Controls

While we believe we have a robust and efficient system of internal and disclosure controls and procedures, our management, including our Chief Executive Officer and Chief Financial Officer, recognize that it is impossible for our disclosure controls and procedures or our internal controls to prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all

control issues and instances of fraud, if any, within our company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act during the three months ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established for “smaller reporting companies.”

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Incorporated by reference from the information in our Proxy Statement for our 2022 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

Item 11. Executive Compensation

Incorporated by reference from the information in our Proxy Statement for our 2022 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Incorporated by reference from the information in our Proxy Statement for our 2022 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Incorporated by reference from the information in our Proxy Statement for our 2022 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

Item 14. Principal Accountant Fees and Services

Incorporated by reference from the information in our Proxy Statement for our 2022 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a)(1) Financial Statements

See the "Index to Consolidated Financial Statements" on page F-1 below for the list of financial statements filed as part of this report.

(a)(2) Financial Statement Schedules

All financial schedules have been omitted because the required information is either presented in the consolidated financial statements filed as part of this Annual Report on Form 10-K or the notes thereto or is not required.

(a)(3) Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
3.1	Restated Certificate of Incorporation of Selecta Biosciences, Inc.	8-K	001-37798	3.1	6/29/2016
3.2	Amended and Restated By-laws of Selecta Biosciences, Inc.	8-K	001-37798	3.2	9/30/2021
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1	333-211555	4.2	5/24/2016
4.2	Form of Warrant to Purchase Shares of Series D Preferred Stock, dated August 9, 2013 or July 25, 2014, issued by the Registrant to Oxford Finance LLC and Square One Bank, together with a schedule of warrant holders	S-1	333-211555	4.5	5/24/2016
4.3	Form of Warrant to Purchase Shares of Series E Preferred Stock, dated December 31, 2015, issued by the Registrant to Oxford Finance LLC and Square One Bank, together with a schedule of warrant holders	S-1	333-211555	4.6	5/24/2016
4.4	Common Stock Purchase Warrant, dated June 27, 2017, by and between the Registrant and Timothy Springer, Ph.D.	8-K	001-37798	4.1	6/28/2017
4.5	Registration Rights Agreement, dated December 23, 2019, by and among the Registrant and the Investors named therein	8-K	001-37798	10.2	12/26/2019
4.6	Registration Rights Agreement, dated as of June 11, 2020, by and between the Registrant and Swedish Orphan Biovitrum AB (Publ)	10-Q	001-37798	4.1	8/6/2020
4.7	Registration Rights Agreement, dated as of June 11, 2020, by and between the Registrant and Swedish Orphan Biovitrum AB (Publ), as amended on November 4, 2020	10-Q	001-37798	4.2	11/5/2020
4.8	Form of Common Stock Purchase Warrant, dated December 23, 2019	8-K	001-37798	4.1	12/26/2019
4.9	Form of Warrant to Purchase Stock, dated August 31, 2020, issued by Selecta Biosciences, Inc. to Oxford Finance LLC and Silicon Valley Bank, together with a schedule of warrants.	8-K	001-37798	4.1	9/3/2020

4.10	Description of Securities	—	—	—	Filed herewith
10.1#	2016 Incentive Award Plan and form of award agreements thereunder	S-1/A	333-211555	10.2	6/8/2016
10.2#	2016 Employee Stock Purchase Plan	S-1/A	333-211555	10.3	6/8/2016
10.3#	2018 Employment Inducement Incentive Award Plan, amended and restated, and forms agreement thereunder	S-8	333-230501	10.1	3/25/2019
10.4#	2008 Stock Incentive Plan and form of award agreements thereunder	S-1/A	333-211555	10.1	6/20/2016
10.5#	Non-Employee Director Compensation Program	10-Q	001-37798	10.2	11/10/2021
10.6#	Form of Indemnification Agreement for Directors and Officers	S-1	333-211555	10.5	5/24/2016
10.7(a)†	Exclusive Patent License Agreement, dated as of November 25, 2008, by and between the Registrant and the Massachusetts Institute of Technology	S-1	333-211555	10.7(a)	5/24/2016
10.7(b)†	First Amendment to Exclusive Patent License Agreement, dated as of January 12, 2010, by and between the Registrant and the Massachusetts Institute of Technology	S-1	333-211555	10.7(b)	5/24/2016
10.7(c)†	Letter Agreement, dated as of November 27, 2012, by and among the Registrant, Massachusetts Institute of Technology and Sanofi	S-1	333-211555	10.7(c)	5/24/2016
10.7(d)†	Letter Amendment, dated as of November 27, 2012, by and between the Registrant and the Massachusetts Institute of Technology	S-1	333-211555	10.7(d)	5/24/2016
10.7(e)†	Second Amendment to Exclusive Patent License Agreement, dated as of August 29, 2013, by and between the Registrant and the Massachusetts Institute of Technology	S-1	333-211555	10.7(e)	5/24/2016
10.7(f)†	Third Amendment to Exclusive Patent License Agreement, entered into on November 21, 2016 and effective as of November 18, 2016, by and between the Massachusetts Institute of Technology and the Registrant	8-K/A	001-37798	10.3(a)	12/14/2016
10.7(g)†	Letter Agreement, dated as of December 2, 2016, by and between the Massachusetts Institute of Technology and the Registrant	8-K/A	001-37798	10.3(b)	12/14/2016
10.7(h)†	Letter Agreement, dated as of December 2, 2016, by and among Spark Therapeutics, Inc., the Massachusetts Institute of Technology and the Registrant	8-K/A	001-37798	10.3(c)	12/14/2016
10.7(i)†	Fourth Amendment to Exclusive Patent License Agreement, entered into on December 13, 2019, by and between the Massachusetts Institute of Technology and the Registrant	10-K	001-37798	10.7(i)	3/12/2020
10.7(j)†	Fifth Amendment to Exclusive Patent License Agreement, dated as of May 15, 2020, by and between the Registrant and the Massachusetts Institute of Technology	10-Q	001-37798	10.1	8/6/2020
10.8†	Amended and Restated License Agreement, dated as of May 31, 2017, by and between the Registrant and Shenyang Sunshine Pharmaceutical Co., Ltd.	10-Q	001-37798	10.6	8/11/2017
10.9†	Manufacturing Services Agreement, dated as of August 1, 2014, by and between the Registrant and Shenyang Sunshine Pharmaceutical Co., Ltd.	S-1	333-211555	10.10	5/24/2016

10.10	Lease Agreement by and between BRE-BMR Grove LLC and Selecta Biosciences, Inc. dated July 23, 2019	10-Q	001-37798	10.3	11/8/2019
10.11#	Employment Agreement, dated as of September 25, 2018, by and between the Registrant and Carsten Brunn, Ph.D.	8-K	001-37798	10.2	9/27/2018
10.12#	Employment Agreement, dated as of June 6, 2016, by and between the Registrant and Takashi Kei Kishimoto	S-1/A	333-211555	10.18	6/8/2016
10.13#	Employment Agreement, dated as of June 6, 2016, by and between the Registrant and Lloyd Johnston, Ph.D.	S-1/A	333-211555	10.21	6/8/2016
10.14#	Employment Agreement, dated as of July 31, 2020, by and between the Registrant and Peter G. Traber, M.D	10-Q	001-37798	10.1	11/5/2020
10.15#	Employment Agreement, dated September 3, 2021, by and between Selecta Biosciences, Inc. and Kevin Tan	10-Q	001-37798	10.1	11/10/2021
10.16†	Stock Purchase Agreement, dated as of December 2, 2016, by and between Spark Therapeutics, Inc. and the Registrant	8-K/A	001-37798	10.2	12/14/2016
10.17†	Feasibility Study and License Agreement by and between Asklepios BioPharmaceutical, Inc. and Selecta Biosciences, Inc. dated August 6, 2019	10-Q	001-37798	10.2	11/8/2019
10.18†	License and Development Agreement, dated as of June 11, 2020, by and between the Registrant and Swedish Orphan Biovitrum AB (Publ)	10-Q	001-37798	10.2	8/6/2020
10.19	Securities Purchase Agreement, dated June 26, 2017, by and between the Registrant and Timothy Springer, Ph.D.	8-K	001-37798	10.2	6/28/2017
10.20	Stock Purchase Agreement, dated August 19, 2019, by and among the Registrant and the Investors named therein	8-K	001-37798	10.1	8/20/2019
10.21(a)	Loan and Security Agreement, dated August 31, 2020, between Selecta Biosciences, Inc., Oxford Finance LLC, as Collateral Agent and as a lender, and Silicon Valley Bank, as a lender.	8-K	001-37798	10.1.1	9/3/2020
10.21(b)	First Amendment to Loan and Security Agreement, dated September 7, 2021, by and among Selecta Biosciences, Inc., Oxford Finance LLC, and Silicon Valley Bank	10-Q	001-37798	10.3	11/9/2021
21.1	Subsidiaries of Selecta Biosciences, Inc.	S-1	333-211555	21.1	5/24/2016
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm	—	—	—	Filed herewith
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	—	—	—	Filed herewith
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	—	—	—	Filed herewith
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	—	—	—	Furnished herewith
101.INS	Inline XBRL Instance Document - the Instance Document does not appear in the interactive data file because its XBRL tags are embedded within the Inline XBRL Document	—	—	—	Filed herewith

101.SCH	Inline XBRL Taxonomy Extension Schema Document	—	—	—	Filed herewith
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	—	—	—	Filed herewith
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	—	—	—	Filed herewith
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	—	—	—	Filed herewith
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	—	—	—	Filed herewith
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)	—	—	—	Filed herewith

# Indicates management contract or compensatory plan.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 24h-2 under the Securities Exchange Act of 1934.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SELECTA BIOSCIENCES, INC.

Date: March 10, 2022

By: /s/ Carsten Brunn, Ph.D.
Carsten Brunn, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Carsten Brunn, Ph.D. Carsten Brunn, Ph.D.	President and Chief Executive Officer, and Director (Principal Executive Officer)	March 10, 2022
/s/ Kevin Tan Kevin Tan	Chief Financial Officer (Principal Financial and Accounting Officer)	March 10, 2022
/s/ Carrie S. Cox Carrie S. Cox	Director	March 10, 2022
/s/ Göran A. Ando, M.D. Göran A. Ando, M.D.	Director	March 10, 2022
/s/ Timothy C. Barabe Timothy C. Barabe	Director	March 10, 2022
/s/ Nishan de Silva, M.D. Nishan de Silva, M.D.	Director	March 10, 2022
/s/ Scott D. Myers Scott D. Myers	Director	March 10, 2022
/s/ Aymeric Sallin Aymeric Sallin	Director	March 10, 2022
/s/ Timothy Springer, Ph.D. Timothy Springer, Ph.D.	Director	March 10, 2022
/s/ Patrick Zenner Patrick Zenner	Director	March 10, 2022

Selecta Biosciences, Inc. and Subsidiaries

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors of Selecta Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Selecta Biosciences, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Revenue Recognition for License and Development Agreement with Swedish Orphan Biovitrum ("Sobi License Agreement")

Description of the Matter

As discussed in Note 12 to the consolidated financial statements, the Company recognized $83.5 million in revenue under the Sobi License Agreement during the year ended December 31, 2021. The Company recognizes revenue for the Combined License Obligation using the output method, based on the proportion of cumulative supply shipped for use in the clinical trials to the Company's estimate of the total supply required during the clinical trial period.

Auditing management's calculation of revenue recognized for the Combined License Obligation under the output method is especially challenging because the assessment of the proportion of cumulative supply shipped required a high degree of audit judgment due to the subjectivity in estimating the remaining supply necessary to satisfy the Combined License Obligation.

How We Addressed the Matter in Our Audit	To audit the Company's revenue recognition for the Combined License Obligation, we performed audit procedures that included, among others, testing the reasonableness of the Company's estimate of the total supply required during the clinical trial period as well as testing the accuracy and completeness of the underlying data used in those estimates. We corroborated management estimates and judgments by reviewing the clinical plans and evaluating the accuracy of the prior period estimates and judgments. We also discussed the estimate of the total supply required during the clinical trial period with the Company's research and development personnel that oversee the activity related to the Sobi License Agreement. Additionally, we performed an independent sensitivity analysis to evaluate the impact on revenues of changes in management's estimate of remaining supply required to satisfy the Combined License Obligation.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2009.

Boston, Massachusetts

March 10, 2022

Selecta Biosciences, Inc. and Subsidiaries
Consolidated Balance Sheets
(Amounts in thousands, except share data and par value)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 114,057	$ 138,685
Marketable securities	13,998	—
Accounts receivable	9,914	7,224
Prepaid expenses and other current assets	6,474	5,434
Total current assets	144,443	151,343
Non-current assets:		
Property and equipment, net	2,142	1,395
Right-of-use asset, net	9,829	10,948
Long-term restricted cash	1,379	1,379
Investments	2,000	—
Other assets	90	370
Total assets	$ 159,883	$ 165,435
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 224	$ 443
Accrued expenses	10,533	8,146
Loan payable	5,961	—
Lease liability	1,049	908
Income taxes payable	601	—
Deferred revenue	53,883	72,050
Total current liabilities	72,251	81,547
Non-current liabilities:		
Loan payable, net of current portion	19,673	24,793
Lease liability, net of current portion	8,598	9,647
Deferred revenue	11,417	38,746
Warrant liabilities	25,423	28,708
Total liabilities	137,362	183,441
Commitments and contingencies (Note 17)		
Stockholders' equity (deficit):		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized; no shares issued and outstanding at December 31, 2021 and December 31, 2020	—	—
Common stock, $0.0001 par value; 200,000,000 shares authorized; 123,622,965 and 108,071,249 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	12	11
Additional paid-in capital	457,391	391,175
Accumulated deficit	(430,316)	(404,629)
Accumulated other comprehensive loss	(4,566)	(4,563)
Total stockholders' equity (deficit)	22,521	(18,006)
Total liabilities and stockholders' equity (deficit)	$ 159,883	$ 165,435

The accompanying notes are an integral part of these consolidated financial statements.

Selecta Biosciences, Inc. and Subsidiaries
Consolidated Statements of Operations and Comprehensive Loss
(Amounts in thousands, except share and per share data)

	Year Ended December 31,		
	2021	**2020**	**2019**
Collaboration and license revenue	$ 85,077	$ 16,597	$ 6,677
Operating expenses:			
Research and development	68,736	54,505	42,743
General and administrative	20,938	18,913	16,389
Total operating expenses	89,674	73,418	59,132
Operating loss	(4,597)	(56,821)	(52,455)
Investment income	44	260	834
Loss on extinguishment of debt	—	(461)	—
Foreign currency transaction gain (loss), net	—	56	(47)
Interest expense	(2,844)	(1,556)	(1,519)
Change in fair value of warrant liabilities	(2,339)	(10,443)	(857)
Other income (expense), net	15	89	(1,306)
Loss before income taxes	(9,721)	(68,876)	(55,350)
Income tax expense	(15,966)	—	—
Net loss	(25,687)	(68,876)	(55,350)
Other comprehensive income (loss):			
Foreign currency translation adjustment	(2)	(40)	34
Unrealized loss on marketable securities	(1)	—	—
Total comprehensive loss	$ (25,690)	$ (68,916)	$ (55,316)
Net loss per share:			
Basic and diluted	$ (0.22)	$ (0.68)	$ (1.22)
Weighted average common shares outstanding:			
Basic and diluted	114,328,798	101,202,176	45,548,511

The accompanying notes are an integral part of these consolidated financial statements.

Selecta Biosciences, Inc. and Subsidiaries
Consolidated Statements of Changes in Stockholders' Equity (Deficit)
(Amounts in thousands, except share data)

	Common stock		Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive loss	Stockholders' Equity (Deficit)
	Shares	Amount				
Balance at December 31, 2018	22,471,776	$ 3	$ 279,539	$ (280,403)	$ (4,557)	$ (5,418)
Issuance of common stock under Employee Stock Purchase Plan	17,205	—	28	—	—	28
Issuance of common stock upon exercise of options	125,600	—	150	—	—	150
Issuance of vested restricted stock units	93,750	—	—	—	—	—
Issuance of common stock, net	22,188,706	2	30,940	—	—	30,942
Issuance of common stock through at-the-market offering, net	615,453	—	1,006	—	—	1,006
Issuance of common stock through private placement	3,178,174	—	5,715	—	—	5,715
Issuance of common stock, pre-funded warrants and warrants through private placement	37,634,883	4	26,125	—	—	26,129
Stock-based compensation expense	—	—	5,161	—	—	5,161
Currency translation adjustment	—	—	—	—	34	34
Net loss	—	—	—	(55,350)	—	(55,350)
Balance at December 31, 2019	86,325,547	$ 9	$ 348,664	$ (335,753)	$ (4,523)	$ 8,397
Issuance of common stock under Employee Stock Purchase Plan	110,212	—	184	—	—	184
Issuance of common stock upon exercise of options	76,128	—	193	—	—	193
Issuance of vested restricted stock units	93,750	—	—	—	—	—
Issuance of common stock through at-the-market offering, net	1,069,486	—	2,108	—	—	2,108
Issuance of common stock through private placement	5,416,390	—	10,268	—	—	10,268
Issuance of common stock upon exercise of pre-funded warrants	8,342,128	1	—	—	—	1
Issuance of common stock upon exercise of warrants	6,637,608	1	24,262	—	—	24,263
Other financing fees	—	—	(370)	—	—	(370)
Issuance of common warrants with long-term debt, net	—	—	444	—	—	444
Stock-based compensation expense	—	—	5,422	—	—	5,422
Currency translation adjustment	—	—	—	—	(40)	(40)
Net loss	—	—	—	(68,876)	—	(68,876)
Balance at December 31, 2020	108,071,249	$ 11	$ 391,175	$ (404,629)	$ (4,563)	$ (18,006)
Issuance of common stock under Employee Stock Purchase Plan	58,794	—	161	—	—	161
Issuance of common stock upon exercise of options	447,492	—	778	—	—	778
Issuance of vested restricted stock units	201,250	—	—	—	—	—
Issuance of common stock through at-the-market offering, net	13,767,511	1	51,933	—	—	51,934
Issuance of common stock upon exercise of warrants	1,076,669	—	5,624	—	—	5,624
Stock-based compensation expense	—	—	7,720	—	—	7,720
Currency translation adjustment	—	—	—	—	(2)	(2)
Unrealized loss on marketable securities	—	—	—	—	(1)	(1)
Net loss	—	—	—	(25,687)	—	(25,687)
Balance at December 31, 2021	123,622,965	$ 12	$ 457,391	$ (430,316)	$ (4,566)	$ 22,521

The accompanying notes are an integral part of these consolidated financial statements.

Selecta Biosciences, Inc. and Subsidiaries
Consolidated Statements of Cash Flows

	Year Ended December 31,		
	2021	2020	2019
Cash flows from operating activities	(Amounts in thousands)		
Net loss	$ (25,687)	$ (68,876)	$ (55,350)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,252	734	726
Amortization of premiums and discounts on marketable securities	57	—	(154)
Non-cash lease expense	1,119	1,127	1,301
Loss on disposal of property and equipment	—	(52)	104
Stock-based compensation expense	7,720	5,422	5,161
Non-cash interest expense	1,012	620	402
Warrant liabilities revaluation	2,339	10,443	857
Loss on extinguishment of debt	—	461	—
Net realized losses on marketable securities	—	—	(1)
Changes in operating assets and liabilities:			
Accounts receivable	(2,690)	(2,224)	(5,000)
Prepaid expenses, deposits and other assets	(1,451)	(4,418)	3,179
Accounts payable	(219)	(57)	(600)
Income taxes payable	601	—	—
Deferred revenue	(45,496)	94,462	337
Accrued expenses and other liabilities	1,061	(2,761)	(2,397)
Net cash (used in) provided by operating activities	(60,382)	34,881	(51,435)
Cash flows from investing activities			
Proceeds from maturities of marketable securities	16,400	—	16,350
Payment made for investments	(2,000)	—	—
Purchases of marketable securities	(30,455)	—	(18,188)
Sales of marketable securities	—	—	1,992
Purchases of property and equipment	(1,085)	(815)	(47)
Proceeds from the sale of property and equipment	—	74	122
Net cash used in investing activities	(17,140)	(741)	229
Cash flows from financing activities			
Proceeds from issuance of long-term debt, net of expenses	—	24,736	—
Repayments of principal on outstanding debt	—	(19,313)	(2,800)
Net proceeds from issuance of common stock	—	—	30,942
Net proceeds from issuance of common stock- at-the-market offering	51,958	2,108	1,006
Net proceeds from issuance of common stock- private placement	—	10,268	5,715
Issuance costs paid for December 2019 financing	—	(4,381)	—
Other financing fees	—	(343)	—
Proceeds from exercise of pre-funded and common warrants	—	979	70,000
Proceeds from exercise of stock options	778	193	150
Proceeds from issuance of common stock under Employee Stock Purchase Plan	161	184	28
Net cash provided by financing activities	52,897	14,431	105,041
Effect of exchange rate changes on cash	(3)	(58)	34
Net change in cash, cash equivalents, and restricted cash	(24,628)	48,513	53,869
Cash, cash equivalents, and restricted cash at beginning of period	140,064	91,551	37,682
Cash, cash equivalents, and restricted cash at end of period	$ 115,436	$ 140,064	$ 91,551
Supplement cash flow information			
Cash paid for interest	$ 2,002	$ 1,018	$ 1,223
Noncash investing and financing activities			
Cashless warrant exercise	$ 5,624	$ 21,790	$ —
Reclassification of warrant liability to equity upon exercise of warrants	$ —	$ 1,494	$ —
Fair value of warrants issued in connection with issuance of long-term debt	$ —	$ 444	$ —
Purchase of property and equipment not yet paid	$ 224	$ 4	$ —
Equity offering costs in accrued liabilities	$ 24	$ 27	$ 4,381
Unrealized loss on marketable securities	$ (1)	$ —	$ —
Debt issuance costs in accrued liabilities	$ —	$ 2	$ —

The accompanying notes are an integral part of these consolidated financial statements.

Selecta Biosciences, Inc. and Subsidiaries
Notes to Consolidated Financial Statements

1. Description of the Business

Selecta Biosciences, Inc., or the Company, was incorporated in Delaware on December 10, 2007, and is based in Watertown, Massachusetts. The Company is a clinical-stage biopharmaceutical company. The Company's ImmTOR® platform encapsulates rapamycin, also known as sirolimus, an FDA approved immunomodulator, in biodegradable nanoparticles ImmTOR is designed to induce antigen-specific immune tolerance. The Company believes, by combining ImmTOR with antigens of interest, the Company's precision immune tolerance platform has the potential to restore self-tolerance to auto-antigens in autoimmune diseases, amplify the efficacy of biologics (including gene therapies) and mitigate the formation of anti-drug antibodies, or ADAs, against biologic drugs.

Since inception, the Company has devoted its efforts principally to research and development of its technology and product candidates, recruiting management and technical staff, acquiring operating assets, and raising capital. The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities.

The Company's product candidates are in development. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, or maintained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees and consultants.

Liquidity and Management's Plan

The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain and sustain profitable operations. The Company is subject to a number of risks similar to other early-stage life science companies, including, but not limited to, successful development of its product candidates, raising additional capital with favorable terms, protection of proprietary technology and market acceptance of any approved future products. The successful development of product candidates requires substantial working capital, which may not be available to the Company on favorable terms or at all.

To date, the Company has financed its operations primarily through the initial public offering of its common stock, private placements of its common stock, issuances of common and preferred stock, debt, research grants, research collaborations and licenses. The Company currently has no source of product revenue, and it does not expect to generate product revenue for the foreseeable future. To date, the Company's revenue has primarily been from collaboration agreements. The Company has devoted substantially all of its financial resources and efforts to developing its ImmTOR platform, identifying potential product candidates and conducting preclinical studies and clinical trials. The Company is in the early stages of development of its product candidates, and it has not completed development of any ImmTOR-enabled therapies.

As of December 31, 2021, the Company's cash, cash equivalents, restricted cash and marketable securities were $129.4 million, of which $1.4 million was restricted cash related to lease commitments and $0.3 million was held by its Russian subsidiary designated solely for use in its operations. The Company believes the cash, cash equivalents, restricted cash and marketable securities as of December 31, 2021 will enable it to fund its current planned operations for at least the next twelve months from the date of issuance of these financial statements, though it may realize additional cash resources upon the achievement of certain contingent collaboration milestones or it may pursue additional cash resources through public or private equity or debt financings or by establishing collaborations with other companies. Management's expectations with respect to its ability to fund current and long term planned operations are based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, the Company may need to seek additional strategic or financing opportunities sooner than would otherwise be expected. However, there is no guarantee that any collaboration milestones will be achieved or that any of these strategic or financing opportunities will be executed on favorable terms, and some could be dilutive to existing stockholders. If the Company is unable to obtain additional funding on a timely basis, it may be forced to significantly curtail, delay, or discontinue one or more of its planned research or development programs or be unable to expand its operations or otherwise capitalize on its commercialization of its product candidates. As of December 31, 2021, the Company had an accumulated deficit of $430.3 million. The Company anticipates operating losses to continue for the

foreseeable future due to, among other things, costs related to research and development of its product candidates and its administrative organization.

At this time, any impact of COVID-19 on the Company's business, revenues, results of operations and financial condition will largely depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the emergence of new virus variants, travel restrictions and social distancing in the United States and other countries, business closures or disruptions, supply chain disruptions, the ultimate impact on financial markets and the global economy, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Guarantees and Indemnifications

As permitted under Delaware law, the Company indemnifies its officers, directors, consultants and employees for certain events or occurrences that happen by reason of the relationship with, or position held at, the Company. Through December 31, 2021, the Company had not experienced any losses related to these indemnification obligations, and no claims were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related reserves were established.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Selecta (RUS), LLC, or Selecta (RUS), a Russian limited liability corporation, and Selecta Biosciences Security Corporation, a Massachusetts securities corporation. All significant intercompany accounts and transactions have been eliminated.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires the Company's management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. The Company's management considers many factors in selecting appropriate financial accounting policies and controls, and bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. In preparing these consolidated financial statements, management used significant estimates in the following areas, among others: revenue recognition, and estimating accrued research and development expenses. The Company assesses the above estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Segment Information

The Company views its operations and manages its business in one operating segment, the research and development of nanoparticle immunomodulatory drugs for the treatment and prevention of human diseases.

Cash Equivalents, Restricted Cash, Marketable Securities and Investments

Cash equivalents include all highly liquid investments maturing within 90 days from the date of purchase. Marketable securities consist of securities with remaining maturities greater than 90 days when purchased. The Company classifies these marketable securities as available-for-sale and records them at fair value in the accompanying consolidated balance sheets. Marketable securities with less than one year until maturity are classified as short term, while marketable securities with maturities greater than one year are classified as long term. Unrealized gains or losses are included in accumulated other comprehensive income (loss). Premiums or discounts from par value are amortized to investment income over the life of the underlying investment. Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses.

We also invest in equity securities of companies whose securities are not publicly traded and where fair value is not readily available. These investments are recorded using cost minus impairment adjusted for changes in observable prices, depending on our ownership percentage and other factors that suggest we have significant influence. We monitor these investments to evaluate whether any increase or decline in their value has occurred, based on the implied value of recent company financings, public market prices of comparable companies and general market conditions. These investments are included in investments and other assets in our consolidated balance sheets.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist primarily of cash, cash equivalents, short-term deposits and marketable securities, investments, and accounts receivable. Cash and cash equivalents are deposited with federally insured financial institutions in the United States and may, at times, exceed federally insured limits.

Management believes that the financial institutions that hold the Company's deposits are financially creditworthy and, accordingly, minimal risk exists with respect to those balances. The Company also maintains cash in Russian bank accounts in denominations of both Russian rubles and U.S. dollars. As of December 31, 2021, the Company maintained approximately $0.3 million in Russian bank accounts, all of which was held in U.S. dollars.

Fair Value of Financial Instruments

The Company's financial instruments consist mainly of cash equivalents, restricted cash, accounts payable, loans payable, marketable securities, investments and common warrants. The carrying amounts of cash equivalents, restricted cash, accounts receivable, and accounts payable approximate their estimated fair value due to their short-term maturities.

Accounting standards define fair value as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. A three-level hierarchy is used to prioritize the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements), and the lowest priority to unobservable inputs (Level 3 measurements). The three levels of the fair value hierarchy are described below:

Level 1—Level 1 inputs are quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date.

Level 2—Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly. If the asset or liability has a specified (contractual) term, a Level 2 input must be observable for substantially the full term of the asset or liability.

Level 3—Level 3 inputs are unobservable inputs for the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date.

To the extent that a valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. The fair value of warrant liabilities is determined using Level 3 inputs.

Fair value is a market-based measure considered from the perspective of a market participant rather than an entity-specific measure. Therefore, even when market assumptions are not readily available, the Company's own assumptions are set to reflect those that market participants would use in pricing the asset or liability at the measurement date. The Company uses prices and inputs that are current as of the measurement date, including during periods of market dislocation. In periods of market dislocation, the observability of prices and inputs may change for many instruments. This condition could cause an instrument to be reclassified within levels in the fair value hierarchy.

The carrying amounts reflected in our consolidated balance sheet for investments approximate fair value, and are assessed for impairment quarterly.

Property and Equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the respective assets, generally seven years for furniture and fixtures, five years for laboratory equipment, software and office equipment and three years for computer equipment. Leasehold improvements are amortized over their useful life or the life of the lease, whichever is shorter. Major additions and betterments are capitalized. Maintenance and repairs, which do not improve or extend the life of the respective assets, are charged to operations as incurred. Costs incurred for construction in progress are recorded as assets and are not amortized until the construction is substantially complete and the assets are ready for their intended use.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. In order to determine if assets have been impaired, assets are tested at the lowest level for which identifiable independent cash flows are available, which is at the entity level ("asset group"). An impairment loss is recognized when the sum of projected undiscounted cash flows is less than the carrying value of the asset group. The measurement of the impairment loss to be recognized is based on the difference between the fair value and the carrying value of the asset group. Based on management's evaluation, the fair value of the asset group, measured as the market capitalization of the Company exceeds its carrying value.

Debt Issuance Costs

Debt issuance costs and fees paid to lenders are classified as a debt discount and are recorded as a direct deduction from the face amount of the related debt. Debt issuance costs are amortized over the term of the related debt using the effective interest method and recorded as interest expense.

Accumulated Other Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in the equity of a business entity during a period from transactions and other events and circumstances from non-owner sources. It includes all changes in equity during a period except those resulting from investments by owners and distributions to owners. Comprehensive income (loss) consists of: (i) all components of net loss and (ii) all components of comprehensive loss other than net loss, referred to as other comprehensive loss. Other comprehensive loss is comprised of unrealized gains and losses on debt securities and foreign currency translation adjustments.

Revenue Recognition

Revenue is recognized when a customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. Pursuant to ASC Topic 606, *Revenue from Contracts with Customers (ASC 606)*, a customer is a party that has contracted with an entity to obtain goods or services that are an output of the entity's ordinary activities in exchange for consideration. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract, including whether they are distinct in the context of the contract; (iii) determine the transaction price, including the constraint on variable consideration; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. If a promised good or service is not distinct, it is combined with other performance obligations. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For example, certain performance obligations associated with Swedish Orphan Biovitrum, or Sobi, Asklepios Biopharmaceutical, Inc., or AskBio, Sarepta Therapeutics, Inc., or Sarepta, and Takeda Pharmaceuticals USA, Inc., or Takeda, (see Note 12) will be satisfied over time, and revenue will be recognized using the output method, based on the proportion of actual deliveries to the total expected deliveries over the initial term.

Collaboration and License Revenue: The Company currently generates its revenue through collaboration and license agreements with strategic collaborators for the development and commercialization of product candidates. Collaboration and license agreements with customers are generally accounted for in accordance with ASC 606. The Company analyzes collaboration arrangements by first assessing whether they are within the scope of ASC Topic 808, *Collaborative Arrangements (ASC 808*), and evaluates whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards that are dependent on the commercial success of such activities. Collaboration agreements with customers that are not within the scope of ASC 808 are accounted for in accordance with ASC 606. To the extent the collaboration agreement is within the scope of ASC 808, the Company also assesses whether any aspects of the agreement are within the scope of other accounting literature (specifically ASC 606). If the Company concludes that some or all aspects of the agreement are distinct and represent a transaction with a customer, the Company accounts for those aspects of the arrangement within the scope of ASC 606. The Company recognizes the shared costs incurred that are not within the scope of other accounting literature as a component of the related expense in the period incurred by analogy to ASC Topic 730, *Research and Development (ASC 730)*, and records reimbursements from counterparties as an offset to the related costs. In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under the agreements in accordance with ASC 606, the Company performs the five steps above. As part of the accounting for the arrangement, the Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include market conditions, reimbursement rates for personnel costs, development timelines and probabilities of regulatory success.

The terms of the Company's arrangements typically include one or more of the following: (i) upfront fees; (ii) milestone payments related to the achievement of development, regulatory, or commercial goals; (iii) royalties on net sales of licensed products; (iv) reimbursements or cost-sharing of research and development (R&D) expenses; and (v) profit/loss sharing arising from co-promotion arrangements.

Licenses of Intellectual Property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. If not distinct, the license is combined with other performance obligations in the contract. For licenses that are combined with other performance obligations, the Company assesses the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. Optional

licenses are evaluated to determine if they are issued at a discount, and therefore, represent material rights and accounted for as separate performance obligations.

Milestone Payments: At the inception of each arrangement that includes developmental and regulatory milestone payments, the Company evaluates whether the achievement of each milestone specifically relates to the Company's efforts to satisfy a performance obligation or transfer a distinct good or service within a performance obligation. If the achievement of a milestone is considered a direct result of the Company's efforts to satisfy a performance obligation or transfer a distinct good or service and the receipt of the payment is based upon the achievement of the milestone, the associated milestone value is allocated to that distinct good or service. If the milestone payment is not specifically related to the Company's effort to satisfy a performance obligation or transfer a distinct good or service, the amount is allocated to all performance obligations using the relative standalone selling price method. The Company also evaluates the milestone to determine whether they are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price to be allocated, otherwise, such amounts are constrained and excluded from the transaction price. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the transaction price. Any such adjustments to the transaction price are allocated to the performance obligations on the same basis as at contract inception. Amounts allocated to a satisfied performance obligation shall be recognized as revenue, or as a reduction of revenue, in the period in which the transaction price changes.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the customer's discretion are evaluated to determine if they are distinct and optional. For optional services that are distinct, the Company assesses if they are priced at a discount, and therefore, provide a material right to the licensee to be accounted for as separate performance obligations.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied) in accordance with the royalty recognition constraint.

Research and Development Costs

Costs incurred in the research and development of the Company's products are expensed as incurred. Research and development expenses include costs incurred in performing research and development activities, including salaries and benefits, stock-based compensation expenses, facilities cost, overhead costs, contract services, supplies and other outside costs. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Clinical Trial Costs

Clinical trial expenses are a significant component of research and development expenses, and the Company outsources a significant portion of these costs to third parties. Third party clinical trial expenses include patient costs, clinical research organization costs and costs for data management. The accrual for site and patient costs includes inputs such as estimates of patient enrollment, patient cycles incurred, clinical site activations, and other pass-through costs. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheets as a prepaid asset or accrued clinical trial cost. These third party agreements are generally cancellable, and related costs are recorded as research and development expenses as incurred. Non-refundable advance clinical payments for goods or services that will be used or rendered for future R&D activities are recorded as a prepaid asset and recognized as expense as the related goods are delivered or the related services are performed. The Company also records accruals for estimated ongoing clinical research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by the Company. The historical clinical accrual estimates made by the Company have not been materially different from the actual costs.

In June 2020, the Company and Sobi entered into a license and development agreement, or the Sobi License. Pursuant to the Sobi License, clinical trial costs incurred to complete development of SEL-212, including but not limited to costs incurred while conducting and completing the Phase 3 DISSOLVE trials, will be reimbursed by Sobi. These costs, when reimbursed, will be recognized as revenue consistent with the revenue recognition methodology disclosed in Note 12. The reimbursable costs exclude any costs of additional development activities required that are related to ImmTOR and that are unrelated to SEL-212.

Income Taxes

The Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax assets to the amount that will more-likely-than-not be realized.

The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more-likely-than-not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes. To date, the Company has not incurred interest and penalties related to uncertain tax positions.

Warrants

The Company determines the accounting classification of warrants that are issued, as either liability or equity, by first assessing whether the warrants meet liability classification in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity*, and then in accordance with ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock*. Under ASC 480, warrants are considered liability classified if the warrants are mandatorily redeemable, obligate the issuer to settle the warrants or the underlying shares by paying cash or other assets, or must or may require settlement by issuing variable number of shares.

If warrants do not meet liability classification under ASC 480-10, the Company assesses the requirements under ASC 815-40, which states that contracts that require or may require the issuer to settle the contract for cash are liabilities recorded at fair value, irrespective of the likelihood of the transaction occurring that triggers the net cash settlement feature. If the warrants do not require liability classification under ASC 815-40, in order to conclude equity classification, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP. After all relevant assessments are made, the Company concludes whether the warrants are classified as liability or equity. Liability classified warrants are required to be accounted for at fair value both on the date of issuance and on subsequent accounting period ending dates, with all changes in fair value after the issuance date recorded in the statements of operations as a gain or loss. Equity classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

Stock-Based Compensation

The Company accounts for all stock-based compensation granted to employees and non-employees using a fair value method. Stock-based compensation is measured at the grant date fair value and is recognized over the requisite service period of the awards, usually the vesting period, on a straight-line basis, net of estimated forfeitures. To the extent that actual forfeitures differ from the Company's estimates, the differences are recorded as a cumulative adjustment in the period the estimates were adjusted. Stock-based compensation expense recognized in the consolidated financial statements is based on awards that ultimately vest.

Net Loss Per Share

The Company calculates basic net loss per share by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding during the period. Diluted net income per share is calculated by dividing the net income attributable to common stockholders by the weighted-average number of common equivalent shares outstanding for the period, including any dilutive effect from outstanding stock options, restricted stock units, warrants to purchase common stock, and employee stock purchase plan stock using the treasury stock method. Given that the Company recorded a net loss for each of the periods presented, there is no difference between basic and diluted net loss per share since the effect of common stock equivalents would be anti-dilutive and are, therefore, excluded from the diluted net loss per share calculation.

Contingent Liabilities

The Company accounts for its contingent liabilities in accordance with ASC No. 450, *Contingencies*. A provision is recorded when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. With respect to legal matters, provisions are reviewed and adjusted to reflect the impact of negotiations, estimated settlements, legal rulings, advice of legal counsel and other information and events pertaining to a particular matter.

Leases

The Company accounts for its leases in accordance with ASC Topic 842, *Leases (ASC 842)*, and determines whether the arrangement is or contains a lease based on the unique facts and circumstances present. Most leases with a term greater than one year are recognized on the balance sheet as right-of-use assets, lease liabilities and, if applicable, long-term lease liabilities. The Company elected not to recognize leases with an original term less than one year on its balance sheet. Operating lease right-of-

use (ROU) assets and their corresponding lease liabilities are recorded based on the present value of lease payments over the expected remaining lease term. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rates, which are the rates incurred to borrow, on a collateralized basis over a similar term, an amount equal to the lease payments in a similar economic environment.

In accordance with the guidance in ASC 842, components of a lease should be split into three categories: lease components (e.g. land, building, etc.), non-lease components (e.g. common area maintenance, consumables, etc.), and non-components (e.g. property taxes, insurance, etc.). Then the fixed and in-substance fixed contract consideration (including any related to non-components) must be allocated based on fair values to the lease components and non-lease components. Although separation of lease and non-lease components is required, the Company elected the practical expedient to not separate lease and non-lease components. The lease component results in an operating right-of-use asset being recorded on the balance sheet and amortized on a straight-line basis as lease expense. Right-of-use assets and operating lease liabilities are remeasured upon certain modifications to leases using the present value of remaining lease payments and estimated incremental borrowing rate upon lease modification.

The Company enters into lease agreements with terms generally ranging from 2-8 years. Some of the Company's lease agreements include Company options to either extend and/or early terminate the lease, the costs of which are included in its operating lease liabilities to the extent that such options are reasonably certain of being exercised. Leases with renewal options allow the Company to extend the lease term typically between 1 and 5 years. When determining the lease term, renewal options reasonably certain of being exercised are included in the lease term. When determining if a renewal option is reasonably certain of being exercised, the Company considers several economic factors, including but not limited to, the significance of leasehold improvements incurred on the property, whether the asset is difficult to replace, underlying contractual obligations, or specific characteristics unique to that particular lease that would make it reasonably certain that the Company would exercise such option. Renewal and termination options were generally not included in the lease term for the Company's existing operating leases. Leases with an initial term of 12 months or less are not recorded on the balance sheet; the Company recognizes lease expense for these leases on a straight-line basis over the lease term.

Recent Accounting Pronouncements

Recently Adopted

In October 2020, the FASB issued ASU 2020-10, *Codification Improvements*, which updates various codification topics by clarifying or improving disclosure requirements to align with the SEC's regulations. The Company adopted the new standard effective January 1, 2021, and there was no impact on its consolidated financial statements.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740) – Simplifying the Accounting for Income Taxes.* ASU 2019-12 simplifies the accounting for income taxes by removing certain exceptions to the general principles in Topic 740. The Company adopted the new standard effective January 1, 2021, and there was no impact on its consolidated financial statements.

Not Yet Adopted

In May 2021, the FASB issued ASU 2021-04, *Earnings Per Share (Topic 260), Debt – Modifications and Extinguishments (Subtopic 470-50), Compensation – Stock Compensation (Topic 718), and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options*. ASU 2021-04 provides guidance as to how entities should account for a modification of the terms or conditions or an exchange of a freestanding equity-classified written call option (i.e., a warrant) that remains equity-classified after modification or exchange as an exchange of the original instrument for a new instrument. An entity should apply the guidance provided in ASU 2021-04 prospectively to modifications or exchanges occurring on or after the effective date. This new standard will be effective for us for fiscal years beginning after December 15, 2021 including interim periods within those fiscal years. The adoption of ASU 2021-04 is not expected to have an impact on the Company's financial position or results of operations upon adoption.

In August 2020, the FASB issued ASU 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40)*. ASU 2020-06 simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. This new standard will be effective for smaller reporting companies for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years. The Company is assessing the impact this standard will have on its consolidated financial statements and disclosures.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326), Measurement of Credit Losses on Financial Instruments*. Subsequently, in November 2018, the FASB issued ASU 2018-19, *Codification Improvements to Topic 326, Financial Instruments-Credit Losses*. ASU 2016-13 requires entities to measure all expected credit losses for most financial assets held at the reporting date based on an expected loss model which includes historical experience, current conditions, and reasonable and supportable forecasts. ASU 2016-13 also requires enhanced disclosures to help financial

statement users better understand significant estimates and judgments used in estimating credit losses. This ASU is effective for smaller reporting companies for fiscal years beginning after December 15, 2022, with early adoption permitted. The adoption of ASU 2016-13 is not expected to have an impact on the Company's financial position or results of operations upon adoption.

3. Marketable Securities and Investments

The following table summarizes the marketable securities held as of December 31, 2021 (in thousands):

	Amortized cost	Unrealized gains	Unrealized losses	Fair value
December 31, 2021				
Corporate bonds	$ 2,007	$ —	$ (1)	$ 2,006
Commercial paper	11,992	—	—	11,992
Total	$ 13,999	$ —	$ (1)	$ 13,998

All marketable securities held at December 31, 2021 had maturities of less than 12 months when purchased and are classified as short-term marketable securities on the accompanying consolidated balance sheet. During the year ended December 31, 2021, there were no marketable securities adjusted for other than temporary declines in fair value. The Company does not intend to sell its investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost bases, which may be maturity. As of December 31, 2021, the Company has a $2.0 million investment in Cyrus pursuant to the Cyrus Agreement. The Company's maximum exposure to loss related to this variable interest entity is limited to the carrying value of the investment. See Note 14 for details.

As of December 31, 2020, the Company held no marketable securities or investments.

4. Net Loss Per Share

The Company has reported a net loss for the years ended December 31, 2021, 2020 and 2019. The Company used the treasury stock method to determine the number of dilutive shares. The following table sets forth the computation of basic and diluted net loss per share (in thousands, except share and per-share data):

	Year Ended December 31,		
	2021	2020	2019
Numerator:			
Net loss	$ (25,687)	$ (68,876)	$ (55,350)
Denominator:			
Weighted-average common shares outstanding - basic and diluted	114,328,798	101,202,176	45,548,511
Net loss per share:			
Basic and diluted	$ (0.22)	$ (0.68)	$ (1.22)

The following table represents the potential dilutive common shares excluded from the computation of the diluted net loss per share for all periods presented, as the effect would have been anti-dilutive:

	Year Ended December 31,		
	2021	2020	2019
Options, RSUs and ESPP shares	11,492,002	7,909,583	7,002,527
Warrants to purchase common stock	10,735,980	12,378,016	23,084,120
Total	22,227,982	20,287,599	30,086,647

5. Fair Value Measurements

The following tables present the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2021 and 2020 (in thousands):

	December 31, 2021			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds (included in cash equivalents)	$ 66,563	$ 66,563	$ —	$ —
Marketable securities:				
Corporate bonds	2,006	—	2,006	—
Commercial paper	11,992	—	11,992	—
Total assets	$ 80,561	$ 66,563	$ 13,998	$ —
Liabilities:				
Warrant liabilities	$ 25,423	$ —	$ —	$ 25,423
Total liabilities	$ 25,423	$ —	$ —	$ 25,423

	December 31, 2020			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds (included in cash equivalents)	$ 80,576	$ 80,576	$ —	$ —
Total assets	$ 80,576	$ 80,576	$ —	$ —
Liabilities:				
Warrant liabilities	$ 28,708	$ —	$ —	$ 28,708
Total liabilities	$ 28,708	$ —	$ —	$ 28,708

There were no transfers within the fair value hierarchy during the years ended December 31, 2021 or 2020.

Cash, Cash Equivalents, and Restricted Cash

As of December 31, 2021 and 2020, the money market funds were classified as cash and cash equivalents on the accompanying consolidated balance sheets as they mature within 90 days from the date of purchase.

As of December 31, 2021, the Company had restricted cash balances relating to a secured letter of credit in connection with its lease for the Company's headquarters (see Note 8 included elsewhere in this Annual Report). The Company's consolidated statement of cash flows includes the following as of December 31, 2021, 2020 and 2019 (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Cash and cash equivalents	$ 114,057	$ 138,685	$ 89,893
Short-term restricted cash	—	—	279
Long-term restricted cash	1,379	1,379	1,379
Total cash, cash equivalents, and restricted cash	$ 115,436	$ 140,064	$ 91,551

Marketable Securities

As of December 31, 2021, marketable securities classified as Level 2 within the valuation hierarchy consist of corporate bonds and commercial paper. Marketable securities represent holdings of available-for-sale marketable debt securities in accordance with the Company's investment policy. The Company estimates the fair value of these marketable securities by taking into consideration valuations that include market pricing based on real-time trade data for the same or similar securities, and other observable inputs. The amortized cost of available-for-sale debt securities is adjusted for amortization of premiums and accretion of discounts to the earliest call date for premiums or to maturity for discounts.

Loans Payable

At December 31, 2021, in light of the recent issuance of the Term A Loan under the 2020 Term Loan, the Company believes the carrying value approximates the fair value of the loan.

Common Warrants

In December 2019, the Company issued common warrants in connection with a private placement of common shares. Pursuant to the terms of the common warrants, the Company could be required to settle the common warrants in cash in the event of certain acquisitions of the Company and, as a result, the common warrants are required to be measured at fair value and reported as a liability on the balance sheet. The Company recorded the fair value of the common warrants upon issuance using the Black-Scholes valuation model and is required to revalue the common warrants at each reporting date with any changes in fair value recorded in the statement of operations and comprehensive loss. The valuation of the common warrants is considered Level 3 of the fair value hierarchy due to the need to use assumptions in the valuation that are both significant to the fair value measurement and unobservable including the volatility rate and the estimated term of the warrants. Generally, increases (decreases) in the fair value of the underlying stock and estimated term would result in a directionally similar impact to the fair value measurement. The changes in the fair values of the Level 3 warrant liability are reflected in the statement of operations and comprehensive loss for the years ended December 31, 2021, 2020 and 2019.

The estimated fair value of warrants is determined using the following inputs to the Black-Scholes simulation valuation:

Estimated fair value of the underlying stock. The Company estimates the fair value of the common stock based on the closing stock price at the end of each reporting period.

Risk-free interest rate. The risk-free interest rate is based on the U.S. Treasury at the valuation date commensurate with the expected remaining life assumption.

Dividend rate. The dividend rate is based on the historical rate, which the Company anticipates will remain at zero.

Expected life. The expected life of the warrants is assumed to be equivalent to their remaining contractual term which expires on December 23, 2024.

Volatility. The Company estimates stock price volatility based on the Company's historical volatility and the historical volatility of peer companies for a period of time commensurate with the expected remaining life of the warrants.

A summary of the Black-Scholes pricing model assumptions used to record the fair value of the warrant liability is as follows:

	December 31,	
	2021	**2020**
Risk-free interest rate	0.97 %	0.36 %
Dividend yield	—	—
Expected life (in years)	2.98	3.98
Expected volatility	96.10 %	98.63 %

Changes in Level 3 Liabilities Measured at Fair Value on a Recurring Basis

The following table reflects a roll-forward of fair value for the Company's Level 3 warrant liabilities (see Note 10), for the year ended December 31, 2021 (in thousands):

	Warrant liabilities
Fair value as of December 31, 2020	$ 28,708
Exercises	(5,624)
Change in fair value	2,339
Fair value as of December 31, 2021	$ 25,423

6. Property and Equipment

Property and equipment consists of the following (in thousands):

	December 31, 2021	December 31, 2020
Laboratory equipment	$ 5,134	$ 4,427
Computer equipment and software	731	532
Leasehold improvements	45	38
Furniture and fixtures	332	327
Office equipment	163	163
Construction in process	534	163
Total property and equipment	6,939	5,650
Less accumulated depreciation	(4,797)	(4,255)
Property and equipment, net	$ 2,142	$ 1,395

Depreciation expense was $0.6 million, $0.6 million and $0.7 million for the years ended December 31, 2021, 2020 and 2019, respectively.

7. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2021	December 31, 2020
Payroll and employee related expenses	$ 3,179	$ 3,049
Collaboration and licensing	—	1,350
Accrued patent fees	309	534
Accrued external research and development costs	4,339	2,029
Accrued professional and consulting services	815	798
Accrued interest	170	170
Other	1,721	216
Accrued expenses	$ 10,533	$ 8,146

Other accrued expenses as of December 31, 2021 include a $0.9 million estimated liability for plaintiff's litigation relating to the two lawsuits described further within Note 17.

8. Leases

65 Grove Street Lease

In July 2019, the Company entered into a lease for 25,078 square feet of laboratory and office space located at 65 Grove Street, Watertown, Massachusetts, or the Headquarters Lease. As part of the Headquarters Lease, the Company incurred $0.8 million in non-reimbursable construction costs. The lease began in March 2020, when the Company took control of the office space, and the lease term is 8 years. The discount rate of 8.9% was determined based on the Company's incremental borrowing rate adjusted for the lease term, including any reasonably certain renewal periods. In connection with the Headquarters Lease, the Company secured a letter of credit from Silicon Valley Bank, or SVB, for $1.4 million, recognized as long-term restricted cash, as of December 31, 2021 and 2020, respectively, which automatically renews each year.

Moscow, Russia Lease

The Company has a month-to-month facility agreement for its Moscow, Russia office. Rent expense is recognized as incurred.

Rent expense for the years ended December 31, 2021, 2020 and 2019 was $2.9 million, $2.7 million, and $2.1 million, respectively.

For the years ended December 31, 2021, 2020 and 2019, the components of lease costs were as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Operating lease cost	2,023	2,096	1,365
Variable lease cost	834	624	828
Short-term lease cost	10	10	16
Total lease cost	$ 2,867	$ 2,730	$ 2,209

The maturity of the Company's operating lease liabilities as of December 31, 2021 were as follows (in thousands):

	December 31, 2021
2022	1,866
2023	1,922
2024	1,980
2025	2,039
2026	2,101
Thereafter	2,844
Total future minimum lease payments	12,752
Less imputed interest	3,105
Total operating lease liabilities	$ 9,647

The supplemental disclosure for the statement of cash flows related to operating leases were as follows (in thousands):

	December 31,	
	2021	2020
Cash paid for amounts included in the measurement of lease liabilities:	$ 1,812	$ 2,523

Other than the initial recording of the right-of-use asset and lease liability for the Headquarters Lease in 2020, which was non-cash, the changes in the Company's right-of-use asset and lease liability for the years ended December 31, 2021 and 2020 are reflected in the non-cash lease expense and accrued expenses and other liabilities, respectively, in the consolidated statements of cash flows.

The following summarizes additional information related to operating leases:

	December 31,	
	2021	2020
Weighted-average remaining lease term	6.4 years	7.4 years
Weighted-average discount rate	8.9 %	8.9 %

9. Debt

2020 Term Loan

On August 31, 2020, the Company entered into a term loan of up to $35.0 million, or the 2020 Term Loan, consisting of term loans in an aggregate amount of $25.0 million, or the Term A Loan, and term loans in an aggregate amount of $10.0 million, or the Term B Loan, governed by a loan and security agreement, or the Loan Agreement, between the Company and Oxford Finance LLC, or Oxford, as Collateral Agent and a Lender, and SVB, as a Lender. The Term A Loan was funded in full on August 31, 2020, or the Funding Date. The second draw period expired on September 30, 2021 and the Term B Loan is no longer available to be drawn by the Company in the future.

The 2020 Term Loan will mature on August 1, 2025. Each advance under the Term Loan accrues interest at a floating per annum rate equal to the greater of (a) 7.90%, and (b) the lesser of (x) the sum of (i) the prime rate reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, and (ii) 4.65% and (y) 10.00%. The Term Loan provides for interest-only payments on a monthly basis until April 1, 2022. Thereafter, amortization payments will be payable monthly in equal installments of principal and interest to fully amortize the outstanding principal over the remaining term of the loan, subject to recalculation upon a change in the prime rate. The Company may prepay the Term Loan in full but not in part provided that the Company (i) provides ten days' prior written notice to Collateral Agent, (ii) pays on the date of such prepayment (A) all outstanding principal plus accrued and unpaid interest, and (B) a prepayment fee of between 3.0% and 1.0% of the aggregate original principal amount advanced by the lender depending on the

timing of the prepayment. Amounts outstanding during an event of default are payable upon SVB's demand and shall accrue interest at an additional rate of 5.0% per annum of the past due amount outstanding. At the end of the loan term (whether at maturity, by prepayment in full or otherwise), the Company shall make a final payment to the lender in the amount of 9.0% of the aggregate original principal amount advanced by the lender. The final payment fee totaling $2.3 million is recorded as a loan discount.

The Term Loan is secured by a lien on substantially all of the assets of the Company, other than intellectual property, provided that such lien on substantially all assets includes any rights to payments and proceeds from the sale, licensing or disposition of intellectual property. The Company has also granted the Collateral Agent a negative pledge with respect to its intellectual property.

The Loan Agreement contains customary covenants and representations, including but not limited to financial reporting obligations and limitations on dividends, indebtedness, collateral, investments, distributions, transfers, mergers or acquisitions, taxes, corporate changes, deposit accounts, and subsidiaries. The Loan Agreement also contains other customary provisions, such as expense reimbursement, non-disclosure obligations as well as indemnification rights for the benefit of the Collateral Agent.

The events of default under the Loan Agreement include, but are not limited to, the Company's failure to make any payments of principal or interest under the Loan Agreement or other transaction documents, the Company's breach or default in the performance of any covenant under the Loan Agreement or other transaction documents, the occurrence of a material adverse change, the Company making a false or misleading representation or warranty in any material respect under the Loan Agreement, the Company's insolvency or bankruptcy, any attachment or judgment on the Company's assets of at least $0.5 million, or the occurrence of any default under any agreement or obligation of the Company involving indebtedness in excess of $0.5 million. If an event of default occurs, the Collateral Agent is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement.

The Company incurred $0.4 million in debt issuance costs in connection with the closing of the 2020 Term Loan. Debt issuance costs are presented in the consolidated balance sheet as a direct deduction from the associated liability and amortized to interest expense over the term of the related debt.

The Company assessed all terms and features of the 2020 Term Loan to identify any potential embedded features that would require bifurcation. As part of this analysis, the Company assessed the economic characteristics and risks of the 2020 Term Loan, including any put, call, and contingent features. The Company determined that the interest rate collar and prepayment call option did not require bifurcation; whereas the contingent put option and default (contingent) interest rate feature met bifurcation criteria resulting in immaterial amounts.

Warrants

On August 31, 2020, in connection with the 2020 Term A Loan, the Company issued warrants to the Lenders to purchase an aggregate of 196,850 shares of its common stock at an exercise price equal to $2.54 per share. In accordance with ASC 815-40, these warrants are classified as permanent equity in the accompanying consolidated balance sheets and will expire ten years from the date of issuance. The initial grant date fair value of the warrants was $0.4 million as determined by the Black-Scholes valuation model and recorded to stockholders' equity, with the SVB portion allocated to the reacquisition price of the 2017 Term Loan and the Oxford fair value portion as a loan discount to the Term A Loan.

Payoff

On the Funding Date, the Company entered into a payoff letter with SVB, pursuant to which the Company utilized $13.7 million of the 2020 Term Loan to pay off all outstanding obligations under the previous term loan, consisting of the principal payment, final prepayment and accrued interest. During the year ended December 31, 2020, the Company recognized a loss on extinguishment of debt in the amount of $0.5 million determined as the difference between the reacquisition price and carrying value at August 31, 2020.

As of December 31, 2021 and 2020, the outstanding principal balance under the 2020 Term Loan was $25.0 million.

Total 2020 Term Loan and unamortized debt discount balances as of December 31, 2021 are as follows (in thousands):

Face value	$	25,000
Venture debt termination fee		2,250
Less: Debt discount		(1,616)
Less: Current portion of loan payable		(5,961)
Loan payable, net of current portion	$	19,673

Future minimum principal payments on the 2020 Term Loan as of December 31, 2021 are as follows (in thousands):

Year ended:		
2022	$	5,488
2023		7,317
2024		7,317
2025		4,878
Total minimum principal payments	$	25,000

During the years ended December 31, 2021, 2020 and 2019, the Company recognized $2.8 million, $1.6 million and $1.5 million respectively of interest expense related to the 2020 and 2017 Term Loans.

10. Equity

Equity Financings

"At-the-Market" Offerings

2017 Sales Agreement and August 2020 Shelf Registration Statement

In August 2017, the Company entered into a sales agreement, or the 2017 Sales Agreement, with Jefferies LLC, as sales agent, to sell shares of its common stock with an aggregate value of up to $50.0 million in an "at the market offering." On August 6, 2020, concurrent with the filing of the updated shelf registration statement, the Company entered into a sales agreement, or the 2020 Sales Agreement with Jefferies LLC, as sales agent, pursuant to which the Company may, from time to time, issue and sell common stock with an aggregate value of up to $50.0 million in an "at the market offering." The 2017 Sales Agreement terminated pursuant to its terms in August 2020. On August 6, 2020, the Company filed an updated universal shelf registration statement on Form S-3 (Reg. No. 333-241692) with the SEC to sell an aggregate amount of up to $200.0 million of certain of its securities. The shelf registration statement was declared effective by the SEC on August 14, 2020. On October 8, 2021, the Company delivered notice to Jefferies LLC that the Company was terminating the 2020 Sales Agreement, with effect as of October 19, 2021.

2021 Sales Agreement

On October 25, 2021, the Company entered into a Sales Agreement, or the 2021 Sales Agreement, with SVB Leerink LLC to sell shares of the Company's common stock, from time to time, through an "at the market" equity offering program under which SVB Leerink will act as sales agent. The shares of common stock sold pursuant to the 2021 Sales Agreement will be issued pursuant to the Company's shelf registration statement on Form S-3 (File No. 333-241692), filed on August 6, 2020 with the Securities and Exchange Commission and related prospectus supplement, filed on October 25, 2021 with the SEC, for aggregate gross sales proceeds of up to $75.0 million.

During the year ended December 31, 2021, the Company sold 13,767,511 shares of its common stock pursuant to the 2021 and 2020 Sales Agreement for aggregate net proceeds of $51.9 million, after deducting commissions and other transaction costs. During the year ended December 31, 2020, the Company sold 1,069,486 shares of its common stock pursuant to the 2020 and 2017 Sales Agreements for aggregate net proceeds of $2.1 million, after deducting commissions and other transaction costs.

June 2020 Sobi Stock Purchase

On June 11, 2020, the Company entered into a stock purchase agreement with Sobi, pursuant to which the Company sold an aggregate of 5,416,390 shares of its common stock at a purchase price equal to $4.6156 per share, which represented 120% of the 10-day volume-weighted average price of the Company's common stock prior to signing, for aggregate gross proceeds of $25.0 million, or the Sobi Private Placement. The closing of the Sobi Private Placement occurred on July 31, 2020.

In accordance with ASC 815, this forward sale treatment qualified as equity classification as the shares are not within the scope of ASC 480. The gross proceeds of $25.0 million were determined to include a premium to the fair value of the Company's shares as of July 28, 2020 of approximately $14.5 million. As a result, such amount was included in the transaction price for revenue recognition of the Sobi License. See Note 12 for details.

Also on June 11, 2020, the Company entered into a registration rights agreement (as amended by that certain letter agreement, dated as of November 4, 2020, the "Sobi Registration Rights Agreement") with Sobi, pursuant to which the Company agreed to prepare and file a registration statement with respect to the resale of the shares of common stock acquired in the Sobi Private Placement. The Company will be required to file this resale registration statement within 30 days following receipt by the Company of a written request from Sobi to file such resale registration statement, and to have the registration statement declared effective within ten (10) Business Days after the SEC informs the Company that no review of such resale registration statement will be made or that the SEC has no further comments on such resale registration statement.

December 2019 Financing

On December 18, 2019, the Company entered into a securities purchase agreement, or the 2019 Purchase Agreement, with a group of institutional investors and certain members of the Board of Directors. Pursuant to the 2019 Purchase Agreement, the Company sold an aggregate of 37,634,883 shares of its common stock at a purchase price of $1.46 per share, warrants to purchase an aggregate of 22,988,501 shares of common stock at a purchase price of $0.125 per share underlying each common warrant, and pre-funded warrants to purchase an aggregate of 8,342,128 shares of common stock at a purchase price of $1.46 per share, all with five year terms, or the 2019 PIPE. The closing of the 2019 PIPE occurred on December 23, 2019. The exercise price of the pre-funded warrants is $0.0001 per share and the exercise price for the common warrants is $1.46 per share. In the event of a certain sale of the Company, the terms of the common warrants require us to make a payment to such common warrant holders based on a Black-Scholes valuation (using variables as specified in the warrants). This provision does not apply to the pre-funded warrants. Therefore, the Company is required to account for the common warrants as liabilities and record them at fair value, while the pre-funded warrants met the criteria to be classified as permanent equity.

The Company recorded the fair value of the common warrants of $40.7 million upon issuance using the Black-Scholes valuation model. Issuance costs were allocated between the equity component with an offset to additional paid-in capital and the liability component recorded as expense on a relative fair value basis. Total net proceeds from the equity offering was $65.6 million, after deducting transaction costs and commissions of $4.4 million.

The common warrants were revalued as of December 31, 2021 at $25.4 million. During the years ended December 31, 2021, 2020 and 2019, the Company recorded a decrease in the fair value of the warrants of $2.3 million, $10.4 million, and $0.9 million, respectively, in the consolidated statements of operations and comprehensive loss.

June 2017 Financing

In June 2017, the Company entered into a securities purchase agreement, or the Institutional Purchase Agreement with a select group of institutional investors, or the Institutional Investors and a securities purchase agreement with Timothy A. Springer, Ph.D., a member of the board of directors, or the Springer Purchase Agreement, for a private placement of the Company's securities, or the 2017 PIPE. Pursuant to the Institutional Purchase Agreement, the Company sold an aggregate of 2,750,000 shares of its common stock at a purchase price equal to $16.00 per share. Pursuant to the Springer Purchase Agreement, the Company sold to Dr. Springer an aggregate of 338,791 shares of common stock at a purchase price equal to $17.71 per share, which was equal to the most recent consolidated closing bid price on the Nasdaq Stock Market on June 23, 2017, and warrants to purchase up to 79,130 shares of common stock, or the Warrant Shares, exercisable at $17.71 per Warrant Share, and with a term of five years. The purchase price for each warrant was equal to $0.125 for each Warrant Share, consistent with Nasdaq Stock Market requirements for an "at the market" offering. Under the terms of the Common Stock Purchase Warrant, the warrants can be settled in unregistered shares. The Warrant Shares qualify for equity classification. The fair value of the allocated proceeds was determined on the relative fair value basis. After deducting for placement agent fees and offering expenses, the aggregate net proceeds from the 2017 PIPE were approximately $47.1 million.

Warrants

During the year ended December 31, 2021, warrant holders exercised 1,642,036 common warrants on a cashless basis and received 1,076,669 shares of common stock.

	Number of Warrants			
	Equity classified	Liability classified	Total	Weighted average exercise price
Outstanding at December 31, 2019	8,437,747	22,988,501	31,426,248	$ 1.12
Exercises	(8,342,128)	(10,902,954)	(19,245,082)	0.83
Issuance	196,850	—	196,850	2.54
Outstanding at December 31, 2020	292,469	12,085,547	12,378,016	$ 1.60
Exercises	—	(1,642,036)	(1,642,036)	1.46
Outstanding at December 31, 2021	292,469	10,443,511	10,735,980	$ 1.62

Common Stock

As of December 31, 2021, the Company had 200,000,000 shares of common stock authorized for issuance, $0.0001 par value per share, with 123,622,965 shares issued and outstanding. The voting, dividend and liquidation rights of the common stockholders are subject to and qualified by the rights, powers and preferences of the preferred stock. The common stock has the following characteristics:

Voting

The common stockholders are entitled to one vote for each share of common stock held with respect to all matters voted on by the stockholders of the Company.

Dividends

The common stockholders are entitled to receive dividends, if and when declared by the Board of Directors. Through December 31, 2021, no dividends have been declared or paid on common stock.

Liquidation

Upon liquidation of the Company, the common stockholders are entitled to receive all assets of the Company available for distribution to such stockholders.

Reserved Shares

The Company has authorized shares of common stock for future issuance as follows:

	As of	
	December 31, 2021	**December 31, 2020**
Exercise of warrants	10,735,980	12,378,016
Shares available for future stock incentive awards	6,039,564	4,916,374
Unvested restricted stock units	394,450	87,500
Outstanding common stock options	11,039,873	7,775,249
Total	28,209,867	25,157,139

11. Stock Incentive Plans

The Company maintains the 2008 Stock Incentive Plan, or the 2008 Plan, for employees, consultants, advisors, and directors. The 2008 Plan provided for the granting of incentive and non-qualified stock option and restricted stock awards as determined by the Board.

In June 2016, the Company's stockholders approved the 2016 Incentive Award Plan, or the 2016 Plan, which authorized 1,210,256 shares of common stock for future issuance under the 2016 Plan and the Company ceased granting awards under the 2008 Plan. Upon the effective date of the 2016 Plan, awards issued under the 2008 Plan remain subject to the terms of the 2008 Plan. Awards granted under the 2008 Plan that expire, lapse or terminate become available under the 2016 Plan as shares available for future grants.

Additionally, pursuant to the terms of the 2016 Plan, the Board is authorized to grant awards with respect to common stock, and may delegate to a committee of one or more members of the Board or executive officers of the Company the authority to grant options and restricted stock units. On December 9, 2020, the Board established a Stock Option Committee authorized to grant awards to certain employees and consultants subject to conditions and limitations within the 2016 Plan. In January 2021 and 2020, the number of shares of common stock that may be issued under the 2016 Plan was increased by 4,322,850 and 3,453,022 shares, respectively. As of December 31, 2021, 1,925,537 shares remain available for future issuance under the 2016 Plan.

In September 2018, the Company's 2018 Employment Inducement Incentive Award Plan, or the 2018 Inducement Incentive Award Plan was adopted by the Board without stockholder approval pursuant to Rule 5635(c)(4) of the Nasdaq Stock Market LLC listing rules, which authorized 1,175,000 shares of its common stock for issuance. In March 2019, the Board approved the amendment and restatement of the 2018 Inducement Incentive Award Plan to reserve an additional 2,000,000 shares of the Company's common stock for issuance thereunder. As of December 31, 2021, there are 1,591,661 shares available for future grant under the 2018 Inducement Incentive Award Plan.

Stock-Based Compensation Expense

Stock-based compensation expense by classification included within the consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Research and development	$ 3,204	$ 2,271	$ 2,079
General and administrative	4,516	3,151	3,082
Total stock-based compensation expense	$ 7,720	$ 5,422	$ 5,161

Stock Options

The estimated grant date fair values of employee stock option awards granted under the 2016 Plan and the 2018 Inducement Incentive Award Plan were calculated using the Black-Scholes option pricing model, based on the following weighted-average assumptions:

	Year Ended December 31,		
	2021	2020	2019
Risk-free interest rate	0.79 %	1.11 %	1.86 %
Dividend yield	—	—	—
Expected term	6.03	6.04	5.94
Expected volatility	95.04 %	91.00 %	87.66 %
Weighted-average fair value of common stock	$ 3.58	$ 2.49	$ 2.01

The weighted average grant date fair value of stock options granted to employees during the years ended December 31, 2021, 2020 and 2019 was $2.73, $1.86, and $1.47 respectively.

As of December 31, 2021 and 2020, total unrecognized compensation expense related to unvested employee stock options was $11.5 million and $8.0 million, respectively, which is expected to be recognized over a weighted average period of 2.7 years and 2.3 years, respectively.

The following table summarizes the stock option activity under the 2008 Plan, 2016 Plan, and 2018 Inducement Incentive Award Plan:

	Number of options	Weighted-average exercise price ($)	Weighted-average remaining contractual term (in years)	Aggregate intrinsic value (in thousands)
Employees				
Outstanding at December 31, 2020	7,302,176	$ 3.98	8.43	$ 4,456
Granted	4,625,611	$ 3.58		
Exercised	(398,754)	$ 1.72		
Forfeited	(912,233)	$ 2.84		
Outstanding at December 31, 2021	10,616,800	$ 3.99	8.19	$ 4,982
Vested at December 31, 2021	4,459,309	$ 4.72	7.23	$ 3,149
Vested and expected to vest at December 31, 2021	9,917,248	$ 4.03	8.13	$ 4,796
Non-employee consultants				
Outstanding at December 31, 2020	473,073	$ 5.89	5.23	$ 86
Exercised	(50,000)	$ 2.04		
Outstanding at December 31, 2021	423,073	$ 6.34	3.85	$ 42
Vested at December 31, 2021	423,073	$ 6.34	3.85	$ 42
Vested and expected to vest at December 31, 2021	423,073	$ 6.34	3.85	$ 42

Restricted Stock Units

During the year ended December 31, 2021, the Company granted 407,700 restricted stock awards with a weighted average fair value of $3.11 per share based on the closing price of the Company's common stock on the date of grant to employees under the 2016 Plan, which will vest over a four year term. Forfeitures are estimated at the time of grant and are adjusted, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The Company has estimated a forfeiture rate of 10% for restricted stock awards to employees based on historical attrition trends. In addition, the Company awarded 197,500 restricted stock units to executives under the 2016 Plan. These restricted stock units vested in two equal installments on the dates applicable performance conditions were achieved during the year ended December 31, 2021.

Unrecognized compensation expense for all restricted stock units was $0.9 million as of December 31, 2021, which is expected to be recognized over a weighted average period of 2.7 years.

The following table summarizes the Company's restricted stock units under the 2016 Plan and 2018 Inducement Incentive Award Plan:

	Number of shares	Weighted average grant date fair value ($)
Unvested at December 31, 2020	87,500	$ 6.03
Granted	605,200	2.10
Vested	(201,250)	1.31
Forfeited	(97,000)	1.76
Unvested at December 31, 2021	394,450	$ 3.45

Employee Stock Purchase Plan

In June 2016, the Company approved the 2016 Employee Stock Purchase Plan, or the ESPP, which authorized 173,076 shares of common stock for future issuance under the ESPP to participating employees. In January 2021 and 2020, the number of shares of common stock authorized for issuance under the ESPP was increased by 1,080,711 shares and 863,254 shares, respectively. During the year ended December 31, 2021, the Company issued 58,794 shares of common stock under the ESPP. As of December 31, 2021, 2,522,366 shares remain available for future issuance under the ESPP.

For each of the years ended December 31, 2021 and 2020, the Company recognized $0.1 million of stock-based compensation expense under the ESPP, respectively.

12. Revenue Arrangements

Takeda Pharmaceuticals USA, Inc.

License and Development Agreement

On October 1, 2021, the Company entered into a License Agreement, or the Takeda Agreement, with Takeda. Under the Takeda Agreement, the Company granted Takeda an exclusive license to the Company's ImmTOR technology initially for two specified disease indications within the field of lysosomal storage disorders. Takeda paid a $3.0 million upfront payment to the Company upon signing of the Takeda Agreement, and the Company is entitled to receive up to $1.124 billion in future additional payments over the course of the partnership that are contingent on the achievement of development or commercial milestones or Takeda's election to continue its activities at specified development stages. The Company is also eligible for tiered royalties on future commercial sales of any licensed products.

Pursuant to the Takeda Agreement, the Company determined the Takeda Agreement represents a service arrangement under the scope of ASC 606, and given the reversion of the rights under the Takeda Agreement represents a penalty in substance for a termination by Takeda, the contract term would remain the stated term of the Takeda Agreement. The Company determined that the research license, the licensed know-how, and the manufactured supply and delivery of materials represent a single promise and performance obligation to be transferred to Takeda over time due to the nature of the promises in the contract. The delivery of the manufactured supply is the predominant promise within the arrangement, as it is essential to the utility of the licensed intellectual property. The material to be supplied by the Company to Takeda is unique to the Company and cannot be obtained by other vendors. As such, consideration in the initial transaction price will be allocated to the single performance obligation and the recognition period would not extend beyond the initial contractual period. The Company will recognize the revenue associated with the upfront payment and combined single performance obligation utilizing the output method over the term that manufactured supply is delivered to Takeda.

In determining the transaction price, the Company concluded the payment associated with all the performance milestones will be fully constrained and only be included in the transaction price when the respective milestone is deemed probable of achievement. Each of these variable consideration items were evaluated under the most likely amount method to determine whether such amounts were probable of occurrence, or whether such amounts should be constrained until they become probable. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt and timing of such study milestones is outside the control of the Company and probability of success criteria is estimated. The Company will re-evaluate the transaction price in each reporting period, as uncertain events are resolved, or as other changes in circumstances occur. Takeda has the right to exercise covenant release rights on a field-by-field basis. If Takeda exercises its covenant release rights, we could receive exercise payments per indication and would be entitled to significant development and commercial milestone payments and tiered royalties on commercial sales. The Company determined that a significant financing component does not exist in its arrangement with Takeda. The Company also determined the options to negotiate additional fields, pursue other products, enter into a supply agreement explore additional fields, and pursue additional development under the initial fields do not represent material rights under the agreement. Takeda has the right to terminate the Takeda Agreement in its entirety or on a field-by-field basis, upon 90 days' written notice to the Company.

As of December 31, 2021, the Company recorded $1.0 million and $1.0 million, as a short-term and long-term contract liabilities, respectively, representing deferred revenue associated with this agreement. Revenue of $1.0 million related to the Takeda Agreement was recognized during the year ended December 31, 2021.

Swedish Orphan Biovitrum

License and Development Agreement

On June 11, 2020, the Company and Sobi entered into the Sobi License. Pursuant to the Sobi License, the Company has agreed to grant Sobi an exclusive, worldwide (except as to Greater China) license to develop, manufacture and commercialize the Company's SEL-212 drug candidate, which is currently in development for the treatment of chronic refractory gout. The SEL-212 drug candidate is a pharmaceutical composition containing a combination of SEL-037, or the Compound, and ImmTOR. Pursuant to the Sobi License, in consideration of the license, Sobi agreed to pay the Company a one-time, upfront payment of $75.0 million. Sobi has also agreed to make milestone payments totaling up to $630.0 million to the Company upon the achievement of various development and regulatory milestones and, if commercialized, sales thresholds for annual net sales of SEL-212, and tiered royalty payments ranging from the low double digits on the lowest sales tier to the high teens on the highest sales tier.

Pursuant to the Sobi License, the Company has agreed to supply (at cost) quantities of the Compound and ImmTOR as necessary for completion of the two Phase 3 clinical trials of SEL-212 (DISSOLVE I and DISSOLVE II) and a 6-month placebo extension. The Company is required to supply quantities of the Compound until all rights to the Compound and any materials needed to manufacture the Compound are transferred to Sobi. Sobi has agreed to reimburse the Company for all budgeted costs incurred to complete development of SEL-212, including but not limited to costs incurred while conducting and completing the Phase 3 DISSOLVE trials, except for any costs of additional development activities required that are related to ImmTOR and that are unrelated to SEL-212. Sobi will have control and responsibility over all regulatory filings, including any investigational drug applications (IND), biologics license applications (BLA), and marketing authorization applications (MAA) relating to the licensed product.

The transactions contemplated by the Sobi License were consummated on July 28, 2020 following the expiration or termination of the required waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976. Sobi may terminate the Sobi License for any reason upon 180 days' written notice to the Company, whereby all rights granted under the Sobi License would revert back to the Company. In addition, if Sobi were to terminate the Sobi License, the Company has the option to obtain a license to all patents and know-how necessary to exploit SEL-212 in existence as of the termination date from Sobi in return for making an equitable royalty payment to Sobi.

Additionally, on June 11, 2020, the Company entered into the Sobi Purchase Agreement in connection with the Sobi License. The closing of the Sobi Private Placement occurred on July 31, 2020, following the closing of the transactions contemplated under the Sobi License. See Note 10 for details.

The Company determined that the Sobi License represents a service arrangement under the scope of ASC 606. In addition, given the Sobi License and Sobi Purchase Agreement were executed contemporaneously and negotiated as a package with a single commercial objective, the Company will account for the two agreements as a single contract. The term of the Sobi License commenced upon the effective date of July 28, 2020 and will continue on a product-by-product basis until the royalty terms for each country have expired. The royalty term for a given product begins upon the first commercial sale of the product in a country and ends at the later of ten years from the first commercial sale, expiration of the last valid patent claim covering the product and expiration of all regulatory exclusivity periods for the product in a country. Given the reversion of the rights under the Sobi License represents a penalty in substance for a termination by Sobi, the contract term would remain the stated term of the Sobi License.

The Company determined that the Sobi License contains three distinct performance obligations due to the nature of the promises in the contract, which includes conducting the Phase 3 DISSOLVE trials, Sobi's option to set-up a second source supplier, and a combined obligation comprised of the delivery of the license to SEL-212, transfer of the know-how and the manufacturing and delivery of SEL-212 supply for development, or the Combined License Obligation. As the set-up of a second source supplier is optional for Sobi and the Company will be reimbursed at cost for its efforts in the subsequent set-up and technology transfer, the option for this future service was determined to be at a significant and incremental discount to its standalone selling price and treated as a material right in the arrangement, namely a distinct performance obligation.

In determining the transaction price, the Company concluded the upfront payment of $75.0 million and the $5.0 million development milestone associated with the dosing of the first patient in the Phase 3 DISSOLVE trials will be included in the transaction price. All other development milestones will be fully constrained and only be included in the transaction price when the respective milestone is deemed probable of achievement. Each of these variable consideration items was evaluated under the most likely amount method to determine whether such amounts were probable of occurrence, or whether such amounts should be constrained until they become probable. As part of the evaluation of the constraint, the Company considered numerous factors, including that receipt of such milestones is outside the control of the Company and probability of success criteria is estimated. The Company will re-evaluate the transaction price in each reporting period, as uncertain events are resolved. In accordance with ASC 606, the Company will only recognize revenue associated with sales-based milestones and royalties when the subsequent sales thresholds are reached and underlying sales occur, respectively. In connection with the Sobi Purchase Agreement, the Company determined that the gross proceeds of $25.0 million from the Sobi Private Placement included a premium to the fair value of the Company's shares as of July 28, 2020 equal to approximately $14.5 million. The premium amount will be included in the transaction price for revenue recognition. The Company will estimate and include in the transaction price the total reimbursements to be received from Sobi for both the manufacturing and delivery of the Compound and ImmTOR as well as conducting the Phase 3 DISSOLVE trials. The Company determined that a significant financing component does not exist in its arrangement with Sobi.

The Company allocated the transaction price based on the relative standalone selling prices of the three distinct performance obligations. The Company estimated the standalone selling price of conducting the Phase 3 DISSOLVE trials by forecasting its anticipated costs and applying a margin reflective of the industry. The Company must determine the standalone selling price of the second source supplier option by determining the discount given to Sobi multiplied by the likelihood that Sobi will exercise the option in the future. Similar to the Phase 3 program estimate, the Company estimated the discount of the option by forecasting the set-up costs and applying a margin that is reflective of the industry. As the Company will be providing the set-up and technology transfer services and the future supply at cost, the discount of the option is equal to the margin amount. The Company considered discussions with Sobi as well as probability of regulatory success of SEL-212 in determining the likelihood of exercise. The Company estimated the standalone selling price of the Combined License Obligation by utilizing a discounted cash flow model.

The Company determined that the delivery of the supply to Sobi best represents the pattern of delivery of the Combined License Obligation as the supply is essential to the utility of the license and know-how. The Company will recognize the revenue allocated to the Combined License Obligation by utilizing the output method. The Company estimated the total supply of the Compound and ImmTOR to be required during the clinical trial period and will recognize revenue as this supply is shipped for use in the clinical trials. The Company will recognize the revenue allocated to the conducting of the Phase 3 DISSOLVE trials obligation by utilizing the input method. The Company estimated the total budgeted costs to be incurred over the Phase 3 DISSOLVE trials and will recognize revenue as these costs are incurred. The Company's costs best represent the pattern of transfer as these will capture all performance of the trials completed to date and can be readily measured. The Company will recognize the revenue allocated to the second source supplier option when the future services and goods are transferred.

As of December 31, 2021 and 2020, the Company recorded $37.5 million and $68.3 million, respectively, as a short-term contract liability and $5.1 million and $24.2 million, respectively, as a long-term contract liability, representing deferred revenue associated with this agreement. In addition, as of December 31, 2021 the Company has recorded $0.7 million of contract assets related to incremental costs that would not have been incurred if the Sobi License had not been obtained, of which $0.6 million is presented in prepaid expenses and other current assets and less than $0.1 million is presented in other assets in the accompanying consolidated balance sheets. Amortization of contract assets was $0.7 million for the year ended December 31, 2021.

As of December 31, 2021 and 2020, the Company recorded a total outstanding receivable of $9.9 million and $6.9 million, respectively, representing billings for the Phase 3 DISSOLVE program that are subject to reimbursement by Sobi. Revenue of $83.5 million and $16.6 million related to the Sobi License was recognized during the years ended December 31, 2021 and 2020, respectively.

Sarepta Therapeutics, Inc.

Research License and Option Agreement

In June 2020, the Company and Sarepta entered into a Research License and Option Agreement, or the Sarepta Agreement. Pursuant to the Sarepta Agreement, the Company agreed to grant Sarepta a license under the Company's intellectual property rights covering the Company's antigen-specific biodegradable nanoparticle encapsulating ImmTOR to research and evaluate ImmTOR in combination with Sarepta's adeno-associated virus gene therapy technology, or gene editing technology, using viral or non-viral delivery, to treat Duchenne Muscular Dystrophy and certain Limb-Girdle Muscular Dystrophy subtypes, or the Indications. Sarepta will have an option term of 24 months during which it can opt-in to obtain an exclusive license to further develop and commercialize the Product to treat at least one Indication, with a potential to extend the option term for an additional fee. The Company will supply ImmTOR to Sarepta for clinical supply on a cost-plus basis.

Sarepta paid a $2.0 million upfront payment to the Company upon signing of the Sarepta Agreement, and the Company is eligible to receive additional preclinical payments during the option term. If Sarepta opts-in to an exclusive license agreement, the Company could receive option exercise payments per Indication upon execution of the exclusive license, and the Company would be entitled to significant development and commercial milestone payments and tiered royalties ranging from the mid-to-high single digits based on net sales.

Pursuant to the Sarepta Agreement, the Company determined the Sarepta Agreement represents a service arrangement under the scope of ASC 606, with a 24 month contract duration. Given the reversion of the rights under the Sarepta Agreement represents a penalty in substance for a termination by Sarepta, the contract term would remain the stated term of the Sarepta Agreement.

The Company determined that the Sarepta Agreement and supply obligation including the delivery of the research license, the licensed know-how, the manufactured supply and delivery of materials represent a single promise and performance obligation to be transferred to Sarepta over time due to the nature of the promises in the contract. The delivery of the manufactured supply is the predominant promise within the arrangement, as it is essential to the utility of the licensed intellectual property. As such, consideration in the initial transaction price will be allocated to the single performance obligation based on the contractual price.

In determining the transaction price, the Company concluded the payment associated with all the performance milestones will be fully constrained and only be included in the transaction price when the respective milestone is deemed probable of achievement. Each of these variable consideration items was evaluated under the most likely amount method to determine whether such amounts were probable of occurrence, or whether such amounts should be constrained until they become probable. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of such study milestones is outside the control of the Company and probability of success criteria is estimated.

The Company also determined the option to enter into a future commercial license agreement and extend the term of the option does not represent a material right since it was not priced at an incremental discount. Sarepta may terminate the Sarepta Agreement for any reason upon 30 days' written notice to the Company. The Sarepta Agreement contains other customary terms and conditions, including representations and warranties, covenants, termination, and indemnification obligations in favor of each party. During the year ended December 31, 2020, the Company and Sarepta entered into two amendments relating to an additional feasibility study. During the year ended December 31, 2021, the Company and Sarepta entered into a third amendment relating to the additional feasibility study.

On April 13, 2021, the Company was notified by Sarepta of the achievement of the milestone event related to the completion of a non-clinical study for Duchenne muscular dystrophy and certain limb-girdle muscular dystrophies under the Sarepta Agreement. Accordingly, the Company received a milestone payment of $3.0 million during the three months ended June 30, 2021.

As of December 31, 2021, two milestones remained constrained, and as of December 31, 2020, all milestones were constrained. The Company will re-evaluate the transaction price in each reporting period, as uncertain events are resolved. The Company will recognize the revenue associated with the upfront payment and combined single performance obligation utilizing the output method, over the 24 month term as the manufactured supply is delivered to Sarepta.

As of December 31, 2021 and 2020, the Company recorded $4.6 million and $2.0 million, respectively, as a short-term contract liability representing deferred revenue associated with this agreement. Revenue of $0.4 million related to the Sarepta Agreement was recognized during the year ended December 31, 2021. De minimis revenue related to the Sarepta License Agreement was recognized during the year ended December 31, 2020.

Asklepios Biopharmaceutical, Inc.

License Agreement for Pompe Disease

In December 2019, the Company and AskBio entered into a license agreement, or the AskBio License Agreement. Pursuant to the AskBio License Agreement, AskBio has exercised its option to exclusively license the Company's intellectual property rights covering the Company's ImmTOR platform to research, develop, and commercialize certain AAV gene therapy products utilizing ImmTOR, and targeting the GAA gene, or derivatives thereof, to treat Pompe Disease.

Pursuant to the AskBio License Agreement and ancillary documents, AskBio agreed to pay to the Company upfront fees of an aggregate of $7.0 million. Assuming successful development and commercialization, the Company could receive up to an additional $237.0 million in development, regulatory, and sales milestone payments. If commercialized, the Company would be eligible to receive tiered royalties on global net sales at percentages ranging from mid-to-high single digits. Under the terms of the agreement, the Company will be eligible to receive these royalties commencing on the first commercial sale of the licensed product until the expiration of the later of (i) ten years after the first commercial sale and (ii) expiration of the last to expire valid claim on patents covering the licensed product.

Pursuant to the AskBio License Agreement, the Company will supply AskBio with its ImmTOR platform, or the Supply Obligation, and AskBio will be responsible for all preclinical, clinical and commercial manufacture and supply of licensed products (other than ImmTOR) and carry out all other activities related to the research, development, and commercialization of licensed products at its sole expense, including all regulatory activities related thereto.

The Company determined that the AskBio License Agreement and Supply Obligation represent a single promise and performance obligation. This is because AskBio cannot derive benefit from the license without the simultaneous transfer of the patent protected ImmTOR supply. Therefore, the License Obligation and Supply Obligation represent the only promise in the arrangement and are combined as a single performance obligation.

In determining the transaction price, the Company concluded that the future development milestones, regulatory milestones, sales milestones, and sales royalties all represent variable consideration. Each of these variable consideration items was evaluated under the most likely amount method to determine whether such amounts were probable of occurrence, or whether such amounts should be constrained until they become probable. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of such milestones is outside the control of the Company. Consideration related to sales-based milestones as well as royalties on net sales upon commercialization by AskBio, will be recognized when the related sales occur, as they were determined to relate predominantly to the intellectual property granted to AskBio and, therefore, have also been excluded from the transaction price in accordance with the royalty recognition constraint. As of December 31, 2021 and 2020, all milestones were constrained. The Company will re-evaluate the transaction price in each reporting period, as uncertain events are resolved, or as other changes in circumstances occur.

The total initial transaction price of the contract on the effective date was $7.0 million, comprised of a $2.0 million initial upfront payment upon agreement of terms, and a $5.0 million initial upfront execution fee.

At each of December 31, 2021 and 2020, the Company recorded $1.7 million as short-term contract liability and $5.3 million as a long-term contract liability, representing deferred revenue associated with this agreement. Revenue will be recognized over the period in which the particles are delivered. No revenue related to the AskBio License Agreement was recognized during the years ended December 31, 2021 and 2020 as no deliveries were made during these periods.

Spark Therapeutics, Inc.

In December 2016, the Company entered into a license and option agreement, or the Spark License Agreement, with Spark pursuant to which the Company and Spark agreed to collaborate on the development of gene therapies for certain targets utilizing the ImmTOR platform. The Spark License Agreement provides Spark with certain exclusive, worldwide, royalty bearing licenses to the Company's intellectual property, allowing Spark to develop and commercialize gene therapies in combination with ImmTOR for Factor VIII, an essential blood clotting protein relevant to the treatment of hemophilia A, the initial target.

Pursuant to the Spark License Agreement, Spark made an upfront payment of $15.0 million. Additionally, in connection with the Spark License Agreement, the Company entered into a Stock Purchase Agreement with Spark. Pursuant to the Spark Purchase Agreement, Spark purchased a total of $15.0 million of the Company's common stock including 197,238 shares for an aggregate purchase price of $5.0 million at the Initial Closing, 324,362 shares of common stock for an aggregate purchase price of $5.0 million on June 8, 2017, and 205,254 shares of common stock from the Company for an aggregate purchase price of $5.0 million on October 31, 2017.

In June 2017, the Company and Spark entered into a letter agreement, or the Letter Agreement, pursuant to which the parties agreed that Spark and the Company agreed to reimburse Spark for all costs and expenses, including the cost of materials provided by the Company, associated with the preclinical research and toxicology studies being performed by Spark for any licensed products for a specified amount of time, or the Reimbursement Period, in an amount not to exceed $2.5 million. In

June 2019, the term of the Reimbursement Period under the Letter Agreement expired. During the year ended December 31, 2019, the Company updated its estimate of variable consideration included in the transaction price to include $1.2 million of unpaid reimbursements to Spark.

In December 2019, the term for Spark to exercise additional target options expired. Therefore, during the year ended December 31, 2019, the Company recognized $6.7 million in revenue. Additionally, during the year ended December 31, 2019, there were two deliveries resulting in less than $0.1 million of revenue recognized. As of December 31, 2020, there was a contract liability of $9.2 million representing long-term deferred revenue to be recognized upon the occurrence of future deliveries under this agreement.

No revenue related to the Spark License Agreement was recognized during the years ended December 31, 2021 and 2020, as no deliveries were made during these periods.

On January 18, 2022, both parties agreed to mutually terminate the Spark License Agreement. Therefore, the contract liability of $9.2 million representing deferred revenue is presented as short-term on the accompanying consolidated balance sheet as of December 31, 2021.

Skolkovo Foundation

During the year ended December 31, 2021, revenue of $0.1 million related to the remaining contract liability of the Russia-based Development Fund of New Technologies Development and Commercialization Center, or Skolkovo, grant funding was recognized at the expiration of the three-year audit period.

Transaction Price Allocated to Future Performance Obligations

Remaining performance obligations represent the transaction price of contracts for which work has not been performed (or has been partially performed). As of December 31, 2021, the aggregate amount of the transaction price allocated to remaining performance obligations was $65.3 million.

Contract Balances from Contracts with Customers (*Takeda, Sobi, Sarepta, AskBio, Spark and Skolkovo*)

The following table presents changes in the Company's contract liabilities during the year ended December 31, 2021 (in thousands):

	Balance at beginning of period	Additions	Deductions	Balance at end of period
Contract liabilities:				
Deferred revenue	$ 110,796	$ 6,000	$ (51,496)	$ 65,300
Total contract liabilities	$ 110,796	$ 6,000	$ (51,496)	$ 65,300

13. Related-Party Transactions

Consulting Services

The Company incurred expenses for consulting services provided by its founders totaling $0.1 million, $0.1 million and $0.5 million during the years ended December 31, 2021, 2020 and 2019, respectively. The Company entered into consulting agreements with its founders to serve on its Scientific Advisory Board, effective January 1, 2020 to December 31, 2021, under which they were paid quarterly for their services.

14. Collaboration and License Agreements

Ginkgo Bioworks Holdings, Inc.

Collaboration and License Agreement

On October 25, 2021, the Company entered into a Collaboration and License Agreement, or the First Ginkgo Agreement, with Ginkgo. Under the First Ginkgo Agreement, Ginkgo will design next generation IgA proteases with potentially transformative therapeutic potential. In return, Ginkgo is eligible to earn both upfront research and development fees and milestone payments, including certain milestone payments for fixed fair values in the form of Selecta common stock, clinical and commercial milestone payments of up to $85.0 million in cash. The Ginkgo Agreement was assessed for collaboration components and was determined not to be within the scope of ASC 808 as the risk and rewards are not shared by both parties. The Company will expense costs related to the Ginkgo Agreement as incurred until regulatory approval is received in accordance with ASC 730. The Company is accounting for the contingently issuable shares to be issued in exchange for the license obtained from Ginkgo as a liability classified stock based compensation arrangement with a non-employee which will be recognized when achievement of the milestones is probable. The Company will assess the capitalization of costs incurred

after the receipt of regulatory approval and, if applicable, will amortize these payments based on the expected useful life of each asset, typically based on the expected commercial exclusivity period. The Company is also obligated to pay Ginkgo tiered royalties ranging from low-single digit to high-single digit percentages of annual net sales of collaboration products which will be expensed as the commercial sales occur.

Genovis AB (publ.)

License Agreement

On October 21, 2021, the Company entered into an Exclusive License Agreement, or the Genovis Agreement, with Genovis. Under the Genovis Agreement, the Company paid to Genovis an upfront payment in exchange for an exclusive license to Genovis' IgG Protease, or Xork, enzyme technology across all therapeutic uses in humans, excluding research, preclinical, diagnostic and other potential non-therapeutic applications of the enzyme. Genovis is eligible to earn development and sales-based milestones. The Genovis Agreement was assessed for collaboration components and was determined not to be within the scope of ASC 808 as the risk and rewards are not shared by both parties. The Company will expense costs related to the Genovis Agreement as incurred until regulatory approval is received in accordance with ASC 730. The Company will assess the capitalization of costs incurred after the receipt of regulatory approval and, if applicable, will amortize these payments based on the expected useful life of each asset, typically based on the expected commercial exclusivity period. The Company is also obligated to pay Genovis tiered royalties of low double digit percentages of worldwide annual net sales of collaboration products which will be expensed as the commercial sales occur.

Cyrus Biotechnology, Inc.

Collaboration and License Agreement

On September 7, 2021, the Company and Cyrus Biotechnology, Inc., or Cyrus, entered into a collaboration and license agreement, or the Cyrus Agreement. Pursuant to the Cyrus Agreement, Cyrus agreed to grant the Company an exclusive, worldwide license to certain intellectual property to form a protein engineering collaboration combining the Company's ImmTOR platform with Cyrus' ability to redesign protein therapeutics. The lead program is a proprietary interleukin-2, or IL-2, protein agonist designed to selectively promote expansion of regulatory T cells for treatment of patients with autoimmune diseases and other deleterious immune conditions. In return for the licensed intellectual property, the Company made an upfront payment and is obligated to pay certain discovery, development, and sales-based milestones which could potentially total up to approximately $1.5 billion across multiple programs. The Cyrus Agreement was assessed for collaboration components and was determined not to be within the scope of ASC 808 as the risk and rewards are not shared by both parties. The Company will expense costs related to the Cyrus Agreement as incurred until regulatory approval is received in accordance with ASC 730. The Company will assess the capitalization of costs incurred after the receipt of regulatory approval and, if applicable, will amortize these payments based on the expected useful life of each asset, typically based on the expected commercial exclusivity period. The Company is also obligated to pay Cyrus tiered royalties ranging from mid-single digit to low-double digit percentages of annual net sales of collaboration products which will be expensed as the commercial sales occur.

Additionally, on September 7, 2021, the Company entered into a stock purchase agreement, or the Series B Preferred Stock Purchase Agreement, in connection with the Cyrus Agreement. Pursuant to the Series B Preferred Stock Purchase Agreement, the Company purchased 2,326,934 shares of Cyrus' Series B Preferred Stock, par value $0.0001 per share, at a purchase price of $0.8595 per share for $2.0 million.

In accordance with ASC 810, the Company has a variable interest in Cyrus resulting from its equity investment. The Company will share in Cyrus' expected losses or receive a portion of its expected returns and absorb the variability associated with changes in the entity's net assets. However, the Company is not the primary beneficiary as it does not have the power to direct the activities most significant to Cyrus, and therefore it is not required to consolidate Cyrus. The Company determined its equity interest to be within the scope of ASC 321 and elected to record the $2.0 million investment of Cyrus' Series B Preferred Stock at cost on the purchase date.

As of December 31, 2021, no impairment indicators are present and therefore the carrying value of the investment in Cyrus is $2.0 million on the accompanying consolidated balance sheet. The Company's maximum exposure to loss related to this variable interest entity is limited to the carrying value of the investment. The Company has not provided financing to Cyrus other than the amount contractually required by the Series B Preferred Stock Purchase Agreement.

Asklepios Biopharmaceutical, Inc.

Feasibility Study and License Agreement

In August 2019, the Company entered into a feasibility study and license agreement with AskBio, or the AskBio Collaboration Agreement. Pursuant to the AskBio Collaboration Agreement, the Company and AskBio agreed to license intellectual property rights to each other as part of a collaboration to research, develop, and commercialize certain AAV gene therapy products utilizing the Company's ImmTOR platform to enable re-dosing of such AAV gene therapy products to treat serious rare and orphan genetic diseases for which there is a significant unmet medical need.

Pursuant to the AskBio Collaboration Agreement, the Company and AskBio agreed to conduct proof of concept studies to potentially validate the use of ImmTOR in conjunction with AskBio's AAV gene therapy, or SEL-302, (previously disclosed as MMA-101, in combination with ImmTOR) for the treatment of MMA, to mitigate the formation of neutralizing anti-AAV capsid antibodies, or the POC Studies. On April 29, 2021, the Company was notified by AskBio that it intended to opt-out of development of the MMA indication. The feasibility study and license agreement with AskBio, or AskBio Collaboration Agreement, otherwise remains in effect. Consequently, the Company has assumed all rights to the MMA program and intends to continue to progress the SEL-302 program through clinical development. The Company filed an IND to conduct a Phase 1/2 clinical trial of its SEL-302 product candidate in pediatric patients with methylmalonic acidemia in the third quarter of 2021. On November 23, 2021, this trial was placed on clinical hold by the FDA, with questions specifically relating to chemistry, manufacturing and controls, or CMC, of the AAV vector. On February 9, 2022, we submitted a written response to the FDA to answer its questions. On March 9, 2022, we received a letter from the FDA indicating the clinical hold was removed and the trial may proceed.

The SEL-399 program combined an empty AAV capsid (EMC-101), which is an AAV capsid containing no transgene, with ImmTOR and is being conducted in partnership with AskBio. Building on the preclinical data the Company has generated showing ImmTOR's effect on mitigating or reducing the formation of neutralizing antibodies to AAV gene therapies, the Company completed a clinical trial of SEL-399 in healthy adult volunteers in Belgium. The goal of the SEL-399 clinical trial was to demonstrate the appropriate dose of ImmTOR in humans to mitigate the formation of antibodies to AAV capsids used in gene therapies. This promising study in healthy volunteers provides support for the potential use of ImmTOR for the inhibition of neutralizing antibodies to AAV8 in gene therapy clinical trials.

The Company and AskBio will share responsibility for the research, development and commercialization of products developed under the SEL-399 program collaboration. The parties will also share research, development, and commercialization costs equally for all collaboration products, but with a right of either party to opt out of certain products, and thereby no longer be required to share costs for such products. Each party will receive a percentage of net profits under the collaboration equal to the percentage of shared costs borne by such party in the development of such product. Pursuant to the AskBio Collaboration Agreement, AskBio is responsible for manufacturing the AAV capsids and AAV vectors and the Company is responsible for manufacturing ImmTOR.

The AskBio Collaboration Agreement is considered to be within the scope of ASC 808, as both parties are active participants and exposed to the risks and rewards of the collaborative activity. The Company evaluated the terms of the AskBio Collaboration Agreement and have identified the following promises in the arrangement (1) conducting research and development activities to develop and commercialize products under the collaboration, or the R&D Services, (2) granting a non-exclusive, non-transferable, royalty-free, fully paid up, worldwide license to certain intellectual property of the Company, or the IP Rights, for the purpose of performing the POC Studies, or the Research License, (3) granting an exclusive, nontransferable, worldwide license to the IP Rights for use in certain indications, or the Collaboration License, (4) providing manufactured supply of preclinical and clinical ImmTOR, or the Manufactured Supply, (5) participation on identified steering committees responsible for the oversight of the collaboration, or the JSC Participation, and (6) granting an exclusive option to obtain a license under the IP Rights to research, develop and commercialize Licensed Products. The Company determined that the R&D Services, Research License, Collaboration License, Manufactured Supply, and JSC Participation were not capable of being distinct, and therefore must be combined into a single performance obligation. Therefore, promises (1) through (5) identified above were combined into a single performance obligation. Furthermore, the Company evaluated the Option Agreement and determined that it does not provide AskBio with a material right under ASC 606 as the option was not priced at a discount (see discussion of the option exercise in Note 12). The Company noted that AskBio did not meet the definition of a customer within the scope of ASC 606 for any distinct performance obligations as the Company concluded that such items were not an output of the Company's ordinary activities. As such, the Company determined that the entire arrangement would be accounted for within the scope of ASC 808. In accordance with ASC 808, collaboration expenses are recognized within R&D expense and selling, general and administrative expense on the Company's condensed consolidated statements of operations.

Under certain collaborative arrangements, the Company is entitled to reimbursement of certain R&D expense. Activities under collaborative arrangements for which the Company is entitled to reimbursement are considered to be collaborative activities under the scope of ASC 808. For these units of account, the Company does not analogize to ASC 606 or recognize revenue. Rather, the Company analogizes to the guidance in ASC 730, which requires that reimbursements from counterparties be recognized as an offset to the related costs. In accordance with ASC 730, the Company records reimbursement payments received from collaborators as reductions to R&D expense.

For the years ended December 31, 2021 and 2020, the Company recognized $2.7 million and $3.8 million, respectively, of collaboration expense under the AskBio Collaboration Agreement in which actual costs incurred by both parties approximate a 50% cost share.

Massachusetts Institute of Technology

In November 2008, the Company entered into an exclusive patent license agreement, or the MIT License, with the Massachusetts Institute of Technology, or MIT, under which the Company received an exclusive royalty-bearing license to utilize patents held by MIT in exchange for upfront consideration and annual license maintenance fees. Such fees are expensed as incurred and have not been material to any period presented.

In June 2020, the Company entered into a Fifth Amendment, or the MIT Amendment, to the MIT License, which is effective as of May 15, 2020. Pursuant to the MIT Amendment, certain of the Company's diligence obligations were extended. The extension included the obligation to commence a Phase 3 trial for a licensed product by the second quarter of 2021 or to file an IND (or equivalent) with the FDA or comparable European regulatory agency for a licensed product by the second quarter of 2023. Additionally, certain of the Company's development and regulatory milestones and payments upon achievement of such milestones were adjusted.

As of December 31, 2021, and in connection with the execution of the Spark License Agreement, the Company has made contractual payments pursuant to the MIT License totaling $2.2 million, and $0.4 million relative to the calculated premium paid by Spark for the equity investments made under the Spark Purchase Agreement. The Company made no additional payments during the year ended December 31, 2021.

Shenyang Sunshine Pharmaceutical Co., Ltd

In May 2014, the Company entered into a license agreement, or the 3SBio License, with Shenyang Sunshine Pharmaceutical Co., Ltd., or 3SBio. The Company has paid to 3SBio an aggregate of $7.0 million in upfront and milestone-based payments under the 3SBio License as of December 31, 2021. The Company is required to make future payments to 3SBio contingent upon the occurrence of events related to the achievement of clinical and regulatory approval milestones of up to an aggregate of $15.0 million for products containing the Company's ImmTOR platform.

15. Income Taxes

The Company provides for income taxes under ASC 740. Under ASC 740, the Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax bases of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse.

On June 11, 2020, the Company entered into the Sobi License (see note 12). In September 2020, Sobi paid the Company a one-time upfront payment of $75.0 million. Sobi has also agreed to make milestone payments totaling up to $630.0 million to the Company upon achievement of various development and regulatory milestones and sales thresholds for annual net sales of SEL-212, and tiered royalty payments ranging from low double digits on the lowest sales tier to high teens on the highest sales tier.

For income tax purposes, the transfer of trademark and product rights is treated as a sale and the net proceeds from the sale are taxed under the default installment method as cash is received by the Company. During the year ending December 31, 2021, the Company completed an analysis of future tax obligations under the default installment sale method versus making a timely filed election on its 2020 tax return due October 15, 2021 to elect out of the installment sale method for income tax purposes. As a result, the Company elected out of the default installment sale treatment with the filing of its tax return. In the elect out method, the Company was taxed based upon the estimated fair value of all present and future proceeds from the sale and the Company utilized all of its available net operating losses and income tax credits, which served to reduce the federal and state tax liability. As the Company recognizes future revenue under the Sobi license for US GAAP purposes, the Company will exclude that revenue from taxable income.

For the year ended December 31, 2021, the Company recognized a current tax expense of $16.0 million, inclusive of estimated penalties and interest of $1.3 million. For the years ended December 31, 2020 and 2019, the Company did not record a current or deferred income tax expense or benefit. The following table reconciles the federal statutory income rate to the Company's effective income tax rate:

	Year Ended December 31,		
	2021	2020	2019
Statutory U.S. federal rate	21.0 %	21.0 %	21.0 %
State income taxes - net of federal benefit	(166.0 %)	5.8 %	6.3 %
Permanent items	8.3 %	(2.9 %)	(2.1 %)
Research tax credits	55.0 %	1.0 %	1.1 %
Deferred revenue	156.5 %	— %	— %
Other	(3.7 %)	— %	— %
Valuation allowance, net	(230.1 %)	(23.6 %)	(26.3 %)
Stock compensation	(5.2 %)	(1.3 %)	— %
Effective income tax rate	(164.2 %)	— %	— %

The tax effects of temporary differences that give rise to the Company's net deferred tax assets are as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Deferred Tax Assets		
Net operating loss carryforwards	$ 13,932	$ 63,678
Research and development credits	1,426	7,632
Stock-based compensations expense	3,955	2,919
Other expenses	745	788
Deferred revenue	102,583	26,699
Operating lease liability	2,636	2,884
Patent costs/amortization	6,843	5,379
Gross deferred tax assets	132,120	109,979
Deferred Tax Liabilities		
Depreciation	$ (90)	$ (11)
Operating lease right-of-use asset	(2,685)	(2,991)
Gross deferred tax liabilities	(2,775)	(3,002)
Net deferred tax assets before valuation allowance	129,345	106,977
Valuation allowance	(129,345)	(106,977)
Net deferred tax assets	$ —	$ —

The Company has provided a full valuation allowance against its net deferred tax assets, as the Company believes that it is more likely than not that the deferred tax assets will not be realized.

Realization of future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets and concluded that it is more likely than not that the Company will not realize the benefit of its deferred tax assets. The valuation allowance increased by $22.4 million and $16.3 million for the years ended December 31, 2021, and 2020, respectively, primarily as a result of an increase in deferred revenue. In 2014, the Company's Russian subsidiary was granted a 10 year tax holiday in Russia. The Company's foreign operations continue to benefit from the tax holiday, which is set to expire on December 31, 2023, however the Company is in the process of closing down operations in Russia and does not expect any tax liability.

At December 31, 2021, the Company has federal and state net operating loss carryforwards of $51.1 million and $50.8 million, respectively, which will expire at various times through 2041. Of the federal net operating losses, $51.1 million can be carried forward indefinitely but will be subject to an 80% limitation. The Company has $1.2 million and $0.3 million, respectively, of federal and state research and development tax credit carryforwards, which will expire at various times through 2041. Utilization of the NOL carryforwards and research and orphan drug credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended (the Code), and similar state law due to ownership changes that could occur in the future.

These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. If the Company experiences a change of control, as defined by Section 382 of the Code and similar state law, utilization of the NOL carryforwards or research and orphan drug credit carryforwards may be subject to an annual limitation under Section 382 of the Code, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required.

Any limitation may result in expiration of a portion of the NOL carryforwards or research and orphan drug credit carryforwards before utilization. The Company performed an analysis of ownership changes through December 31, 2021. Based on this analysis, the Company does not believe that any of its tax attributes through December 31, 2021 will expire unutilized due to Section 382 limitations.

The Company applies ASC 740, *Income Taxes* to uncertain tax positions. As of the adoption date on January 1, 2010 and through December 31, 2021, the Company had no unrecognized tax benefits or related interest and penalties accrued.

During 2021, the Company completed a detailed study of its research and development and orphan drug credits through December 31, 2020. As a result, the Company adjusted its current tax payable and deferred tax asset balances and the impacts are included in the federal research and orphan drug credit and state income taxes lines in the effective rate reconciliation above.

Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying statement of operations. As of December 31, 2021, the Company had no accrued interest related to uncertain tax positions.

The statute of limitations for assessment by the Internal Revenue Service and Massachusetts tax authorities is open for tax years since inception as the Company claimed research tax credits on its 2020 tax return which remains open for examination for the 2020 year as well as for any year in which a credit has been claimed for. The Company files income tax returns in the United States and Massachusetts. There are currently no federal, state or foreign audits in progress.

16. Defined Contribution Plan

The Company maintains a defined contribution plan, or the 401(k) Plan, under Section 401(k) of the Internal Revenue Code. The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax basis. The 401(k) Plan provides for matching contributions on a portion of participant contributions pursuant to the 401(k) Plan's matching formula. All matching contributions vest ratably over four years and participant contributions vest immediately. Contributions by the Company totaled $0.2 million, $0.1 million, and $0.1 million during each of the years ended December 31, 2021, 2020 and 2019, respectively.

17. Commitments and Contingencies

As of December 31, 2021, the Company was not a party to any litigation that could have a material adverse effect on the Company's business, financial position, results of operations or cash flows.

On August 3, 2020, a stockholder of Selecta filed a stockholder derivative action, purportedly on behalf of Selecta and against certain current and former members of the Company's Board of Directors, as well as one affiliated company owned by a current board member, in the Court of Chancery of the State of Delaware, namely Franchi v. Barabe, et al. The complaint alleges that the individual defendants breached their fiduciary duties and committed corporate waste when they authorized a private placement transaction, announced on December 19, 2019, at a price allegedly below fair value. The complaint further alleges that the four defendant directors who participated in the private placement were unjustly enriched in connection with the transaction. On September 25, 2020, the defendants filed a motion to dismiss the lawsuit. On November 6, 2020, the plaintiff filed an amended complaint, and the defendants filed a second motion to dismiss on January 8, 2021. On December 31, 2020, we received a litigation demand letter from two other putative stockholders relating to the same private placement transaction. On April 12, 2021, the Court of Chancery in the State of Delaware granted a motion to stay the litigation pending a review by a Special Committee appointed by the Company's Board of Directors. While the litigation was stayed, the parties reached an agreement in principle to settle the matter, and they expect to submit documentation to the Court for its approval of the settlement in the near future. As of December 31, 2021, the Company accrued an estimated liability of $0.9 million for the plaintiff's litigation, as the liability has been determined to be probable.

Other

As permitted under Delaware law, the Company indemnifies its directors for certain events or occurrences while the director is, or was, serving at the Company's request in such capacity. The term of the indemnification is for the director's lifetime. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors' insurance coverage that limits its exposure and enables it to recover a portion of any future amounts paid. The Company also has indemnification arrangements under certain of its facility leases that require it to indemnify the landlord against certain costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from certain breaches, violations, or non-performance of any covenant or condition of the Company's lease. The term of the indemnification is for the term of the related lease agreement. The maximum potential amount of future payments the Company could be

required to make under these indemnification agreements is unlimited. To date, the Company had not experienced any material losses related to any of its indemnification obligations, and no material claims with respect thereto were outstanding.

The Company is a party in various other contractual disputes and potential claims arising in the ordinary course of business. The Company does not believe that the resolution of these matters will have a material adverse effect the Company's business, financial position, results of operations or cash flows.

18. Subsequent Events

Collaboration and License Agreements

On January 3, 2022, the Company entered into a Collaboration and License Agreement with Ginkgo Bioworks, Inc, or the Second Ginkgo Agreement. Under this agreement, the Company will engage with Ginkgo to develop AAV capsids designed to enhance transduction efficiency and transgene expression. In return, Ginkgo is eligible to earn both upfront research and development fees and milestone payments, including certain milestone payments in the form of Selecta common stock, clinical and commercial milestone payments of up to $207 million in cash, as well as downstream value in the form of royalties on sales.

"At-the-Market" Offerings

Subsequent to December 31, 2021, the Company sold 576,418 shares of its common stock pursuant to the 2021 Sales Agreement for aggregate net proceeds of $1.7 million, after deducting commissions and other transaction costs.

Exhibit 31.1

CERTIFICATIONS

I, Carsten Brunn, Ph.D. certify that:

1. I have reviewed this Annual Report on Form 10-K of Selecta Biosciences, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

March 10, 2022

/s/ Carsten Brunn, Ph.D.

Carsten Brunn, Ph.D.

President and Chief Executive Officer, and Director

(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Kevin Tan, certify that:

1. I have reviewed this Annual Report on Form 10-K of Selecta Biosciences, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

March 10, 2022

/s/ Kevin Tan

Kevin Tan
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Selecta Biosciences, Inc. (the "Company") for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

1. The Annual Report on Form 10-K of the Company for the period ended December 31, 2021 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

March 10, 2022

/s/ Carsten Brunn, Ph.D.
Carsten Brunn, Ph.D.
President and Chief Executive Officer, and Director
(Principal Executive Officer)

March 10, 2022

/s/ Kevin Tan
Kevin Tan
Chief Financial Officer
(Principal Financial Officer)

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8, File No. 333-212215) pertaining to the 2008 Stock Incentive Plan, as amended, the 2016 Incentive Award Plan and the 2016 Employee Stock Purchase Plan of Selecta Biosciences, Inc.,

(2) Registration Statement (Form S-8, File No. 333-224109) pertaining to the 2016 Incentive Awards Plan and the 2016 Employee Stock Purchase Plan of Selecta Biosciences, Inc.,

(3) Registration Statement (Form S-8, File No. 333-228264) pertaining to the 2018 Employment Inducement Incentive Award Plan of Selecta Biosciences, Inc.,

(4) Registration Statement (Form S-8, File No. 333-230501) pertaining to the 2018 Employment Inducement Incentive Award Plan of Selecta Biosciences, Inc.,

(5) Registration Statement (Form S-8, File No. 333-239075) pertaining to the 2016 Incentive Award Plan and the 2016 Employee Stock Purchase Plan of Selecta Biosciences, Inc.,

(6) Registration Statement (Form S-8, File No. 333-256061) pertaining to the 2016 Incentive Award Plan and the 2016 Employee Stock Purchase Plan of Selecta Biosciences, Inc.,

(7) Registration Statement (Form S-3, File No. 333-236147) of Selecta Biosciences, Inc., and

(8) Registration Statement (Form S-3, File No. 333-241692) of Selecta Biosciences, Inc.;

of our report dated March 10, 2022 with respect to the consolidated financial statements of Selecta Biosciences, Inc. included in this Annual Report (Form 10-K) of Selecta Biosciences, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 10, 2022

Exhibit 4.10

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

As of December 31, 2021, Selecta Biosciences, Inc. (the "Company," "we," "us" and "our") had one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended: our common stock, par value $0.0001 per share ("common stock").

The following description of our common stock is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to our Restated Certificate of Incorporation (the "Certificate"), our Amended and Restated Bylaws (the "Bylaws") and applicable provisions of the Delaware General Corporation Law ("DGCL"). Our Certificate and Bylaws are included as exhibits to the Annual Report on Form 10-K of which this Exhibit 4.10 forms a part. We encourage you to carefully read our Certificate, Bylaws and the applicable provisions of the DGCL for additional information.

General

Under the Certificate, we have the authority to issue 200,000,000 shares of common stock. Our common stock is listed on The Nasdaq Global Market under the symbol "SELB." The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock we may designate and issue in the future.

Common Stock Outstanding

The outstanding shares of our common stock are duly authorized, validly issued, fully paid and nonassessable.

Voting Rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our Certificate and Bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least a majority of the voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our Certificate.

Rights Upon Liquidation

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock.

Dividend Rights

Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

Other Rights

Holders of common stock have no preemptive, subscription, redemption or conversion rights.

Registration Rights

Certain holders our common stock or their transferees are entitled to the following rights with respect to the registration of such shares for public resale under the Securities Act of 1933, as amended (the "Securities Act").

These registration rights are granted pursuant to (i) a registration rights agreement, or the 2019 Registration Rights Agreement, we entered into in connection with the private placement of 37,634,883 shares of our common stock and warrants to purchase 31,330,629 shares of our common stock, or the 2019 Private Placement, which closed on December 23, 2019; and (ii) a registration rights agreement, or the 2020 Registration Rights Agreement, we entered into in connection with the private placement of 5,416,390 shares of our common stock, or the 2020 Private Placement, which closed on July 31, 2020.

2019 Registration Rights Agreement

The shares of common stock underlying the warrants and the shares of common stock issued in connection with our 2019 Private Placement are currently registered under a registration statement that has been declared effective by the SEC, pursuant to the 2019 Registration Rights Agreement. Subject to certain exceptions, pursuant to the 2019 Registration Rights Agreement, we have agreed to use reasonable best efforts to keep the registration statement registering the resale of these shares of common effective under the Securities Act until the earlier of (i) such time as all of the securities registered for resale have been disposed of pursuant to and in accordance with the registration statement, (ii) such time as all of the securities registered for resale have been sold in accordance with Rule 144 under the Securities Act, (iii) the date on which the shares of common stock registered for resale become eligible for resale without volume or manner-of-sale restrictions and without current public information pursuant to Rule 144; and (iv) December 23, 2024.

We have also agreed, among other things, to indemnify the investors under the registration statement from certain liabilities and to pay all fees and expenses (excluding any legal fees of the selling holder(s), and any underwriting discounts and selling commissions) incident to our obligations under the 2019 Registration Rights Agreement.

2020 Registration Rights Agreement

Holders of registrable securities under the 2020 Registration Rights Agreement, as amended, have registration rights until the earlier of (i) such time as there are no longer any registrable securities held by the purchaser, its affiliates or permitted transferees and (ii) such time as all of the securities can otherwise be sold without regard to the volume or manner-of-sale restrictions pursuant to Rule 144. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Piggyback Registration Rights. Any time we propose to register any shares of our common stock under the Securities Act, subject to certain exceptions, the holders of registrable securities are entitled to notice of the registration and to include their shares of registrable securities in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Demand Registration Rights. If the holders of registrable securities request in writing that we effect a registration with respect to all of the registrable securities, we will be required to effect such registration.

Expenses. Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling security holders and blue sky fees and expenses.

Termination of Registration Rights. The registration rights terminate upon the earlier of (i) such time as there are no longer any registrable securities held by the purchaser, its affiliates or permitted transferees and (ii) such time as all of the securities can otherwise be sold without regard to the volume or manner-of-sale restrictions pursuant to Rule 144.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of the DGCL, our Certificate and our Bylaws could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interest, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock. The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to effect a change in control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings. Our Bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president (in the absence of a chief executive officer), or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals. Our Bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent. Our Certificate eliminates the right of stockholders to act by written consent without a meeting.

Staggered Board. Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors. Our Certificate provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting. Our Certificate does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute. We are subject to Section 203 of the DGCL, which prohibits persons deemed to be “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this law may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum. Our Certificate provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our Certificate or Bylaws; or (4) any action asserting a claim governed by the internal affairs doctrine. Our Certificate also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our Certificate is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of Certificate. The amendment of any of the above provisions in our Certificate, except for the provision making it possible for our board of directors to issue preferred stock and the provision prohibiting cumulative

voting, would require approval by holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote thereon.

The provisions of the DGCL, our Certificate and our Bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interest.