Protalix BioTherapeutics, Inc.
Form 10-K
March 06, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d)

OF THE SECURITIES EXCHANGE ACT OF 1934

(Mark One)

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

For the fiscal year ended December 31, 2017

OR

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

For the transition period from _____ to _____

001-33357

(Commission file number)

PROTALIX BIOTHERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**65-0643773**
State or other jurisdiction of incorporation or organization	**(I.R.S. Employer Identification No.)**
2 Snunit Street Science Park POB 455 Carmiel, Israel	**20100**
(Address of principal executive offices)	**(Zip Code)**

972-4-988-9488

Registrant's telephone number, including area code

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

Title of each class	**Name of each exchange on which registered**
Common stock, par value $0.001 per share	**NYSE AMERICAN**

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 ¨ No x

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 ¨ No x

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 x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

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

Large accelerated filer ¨	Accelerated filer x
Non-accelerated filer ¨(Do not check if a smaller reporting company)	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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

The aggregate market value of the voting common equity held by non-affiliates of the Registrant, as of June 30, 2017 was approximately $105.4 million, based upon a per share price equal to $0.84, the closing price for shares of the Registrant's common stock reported by the NYSE American for such date.

On March 1, 2018, approximately 145,569,955 shares of the Registrant's common stock, par value $0.001 per share, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for its 2018 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission no later than May 1, 2018 and to be delivered to shareholders in connection with the 2018 Annual Meeting of Stockholders, are herein incorporated by reference in Part III of this Form 10-K.

FORM 10-K

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PART I

Except where the context otherwise requires, the terms, "we," "us," "our" or "the Company," refer to the business of Protalix BioTherapeutics, Inc. and its consolidated subsidiaries, and "Protalix" or "Protalix Ltd." refers to the business of Protalix Ltd., our wholly-owned subsidiary and sole operating unit.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

The statements set forth under the captions "Business," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Risk Factors," and other statements included elsewhere in this Annual Report on Form 10-K, which are not historical, constitute "forward-looking statements" within the meanings of 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, including statements regarding expectations, beliefs, intentions or strategies for the future. When used in this report, the terms "anticipate," "believe," "estimate," "expect," "can," "continue," "could," "intend," "plan," "potential," "predict," "project," "should," "will," "would" and other words or phrases of similar import, as they relate company or our subsidiaries or our management, are intended to identify forward-looking statements. We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are only predictions and reflect our views as of the date they are made with respect to future events and financial performance, and we undertake no obligation to update or revise, nor do we have a policy of updating or revising, any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events, except as may be required under applicable law. Forward-looking statements are subject to many risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements.

Examples of the risks and uncertainties include, but are not limited to, the following:

- failure or delay in the commencement or completion of our preclinical studies and clinical trials, which may be caused by several factors, including: slower than expected rates of patient recruitment; unforeseen safety issues; determination of dosing issues; lack of effectiveness during clinical trials; inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; inability to monitor patients adequately during or after treatment; and or lack of sufficient funding to finance our clinical trials;

- the risk that the results of our clinical trials will not support the applicable claims of superiority, safety or efficacy and that our product candidates will not have the desired effects or will have undesirable side effects or other unexpected characteristics;

- risks relating to our ability to manage our relationship with Chiesi Farmaceutici S.p.A., or Chiesi, and any other collaborator, distributor or partner;

- risks relating to our ability to make scheduled payments of the principal of, to pay interest on or to refinance or satisfy conversions of our outstanding convertible notes or any other indebtedness;

- risks relating to our ability to defease the remaining outstanding 4.5% convertible notes on or prior to June 16, 2018;

- risks relating to the compliance by Fundação Oswaldo Cruz, or Fiocruz, an arm of the Brazilian Ministry of Health, or the Brazilian MoH, with its purchase obligations under our supply and technology transfer agreement, which may have a material adverse effect on our company and may also result in the termination of such agreement;

- our dependence on performance by third-party providers of services and supplies, including without limitation, clinical trial services;

- risks relating to our ability to finance our research programs;

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- delays in preparing and filing applications for regulatory approval of our product candidates in the United States, the European Union and elsewhere;

- the impact of development of competing therapies and/or technologies by other companies;

- the risk that products that are competitive to our product candidates may be granted orphan drug status in certain territories and, therefore, one or more of our product candidate may become be subject to potential marketing and commercialization restrictions;

- risks related to our supply of drug product to Pfizer Inc., or Pfizer, pursuant to our amended and restated exclusive license and supply agreement with Pfizer;

- risks related to the commercialization efforts for taliglucerase alfa in Brazil;

- risks related to our expectations with respect to the potential commercial value of our product and product candidates;

- the inherent risks and uncertainties in developing the types of drug platforms and products we are developing;

- potential product liability risks, and risks of securing adequate levels of product liability and clinical trial insurance coverage;

- the possibility of infringing a third party's patents or other intellectual property rights;

- the uncertainty of obtaining patents covering our products and processes and in successfully enforcing our intellectual property rights against third parties;

- risks relating to changes in healthcare laws, rules and regulations in the United States or elsewhere; and

- the possible disruption of our operations due to terrorist activities and armed conflict, including as a result of the disruption of the operations of regulatory authorities, our subsidiaries, our manufacturing facilities and our customers, suppliers, distributors, collaborative partners, licensees and clinical trial sites.

Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced or late-stage clinical trials, even after obtaining promising earlier trial results or preliminary findings for such clinical trials. Even if favorable testing data is generated from clinical trials of a drug product, the U.S. Food and Drug

Administration, or the FDA, or foreign regulatory authorities may not accept or approve a marketing application filed by a pharmaceutical or biotechnology company for the drug product.

These forward-looking statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These and other risks and uncertainties are detailed under the heading “Risk Factors” in this Annual Report and are described from time to time in the reports we file with the U.S. Securities and Exchange Commission, or the Commission.

Item 1. Business

We are a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins based on our proprietary ProCellEx® protein expression system. We developed our first commercial drug product, Elelyso®, using our ProCellEx system and we are now focused on utilizing the system to develop a pipeline of proprietary, clinically superior versions of recombinant therapeutic proteins that primarily target large, established pharmaceutical markets and that in most cases rely upon known biological mechanisms of action. With our experience to date, we believe ProCellEx will enable us to develop additional proprietary recombinant proteins that are therapeutically superior to existing recombinant proteins currently marketed for the same indications, including applying the unique properties of our ProCellEx system for the oral delivery of therapeutic proteins.

The following table summarizes our current product candidates and their respective stages of clinical development:

On October 19, 2017, Protalix Ltd., our wholly-owned subsidiary, and Chiesi entered into an Ex-US license and collaboration agreement, which we refer to as the Chiesi Agreement, pursuant to which Chiesi was granted an exclusive, license for all markets outside of the United States to develop and commercialize pegunigalsidase alfa. Pegunigalsidase alfa, or PRX-102, is our chemically modified version of the recombinant protein alpha-Galactosidase-A protein that is currently being evaluated in phase III clinical trials for the treatment of Fabry disease. Under the terms and conditions of the Chiesi Agreement, Protalix Ltd. retained the right to commercialize pegunigalsidase alfa in the United States. Under the Chiesi Agreement, Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to $25 million in development costs, capped at $10 million per year. Protalix Ltd. is also eligible to receive an additional up to $320 million, in the aggregate, in regulatory and commercial milestone payments. Protalix Ltd. and Chiesi have agreed to a specific allocation of the responsibilities for the continued development efforts for pegunigalsidase alfa. Protalix Ltd. will manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi will make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa. The Chiesi Agreement also provides for reimbursement by Chiesi of certain costs to be incurred by Protalix Ltd.

In December 2017, the European Commission granted Orphan Drug Designation for pegunigalsidase alfa for the treatment of Fabry disease. The designation was granted after the EMA's Committee for Orphan Medicinal Products, or the COMP, issued a positive opinion supporting the designation noting that we had established that there was medically plausible evidence that pegunigalsidase alfa will provide a significant benefit over existing approved therapies in the European Union for the treatment of Fabry disease. The COMP cited clinical and non-clinical justifications we provided to establish the significant benefit of pegunigalsidase alfa, noting that the COMP considered the justifications to constitute a clinically relevant advantage. Orphan Drug Designation for pegunigalsidase alfa qualifies Protalix Ltd. for access to a centralized marketing authorization procedure, including applications for inspections and for protocol assistance. If the orphan drug designation is maintained at the time pegunigalsidase alfa is approved for marketing in the European Union, if at all, we expect that PRX-102 will benefit from 10 years of market exclusivity within the European Union. The market exclusivity will not have any effect on Fabry disease treatments already approved at that time.

In January 2018, FDA granted Fast Track designation to PRX-102. Fast Track designation is a process designed to facilitate the development and expedite the review of drugs and vaccines for serious conditions that fill an unmet medical need.

On May 1, 2012, the FDA approved for sale our first commercial product, taliglucerase alfa for injection, an enzyme replacement therapy, or ERT, for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease. Subsequently, taliglucerase alfa was approved for marketing by the regulatory authorities of other countries. Taliglucerase alfa is called alfataliglicerase in Brazil and certain other Latin American countries, where it is marketed under the name alfataliglicerase. Taliglucerase alfa is marketed under the name Elelyso in other territories.

Since its approval by the FDA, taliglucerase alfa has been marketed by Pfizer, as provided in the exclusive license and supply agreement by and between Protalix Ltd. and Pfizer, which we refer to as the Pfizer Agreement. In October 2015, we entered into an Amended and Restated Exclusive License and Supply Agreement, or the Amended Pfizer Agreement, which amends and restates the Pfizer Agreement in its entirety. Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso in exchange for a cash payment equal to $36.0 million. As part of the sale, we agreed to transfer our rights to Elelyso in Israel to Pfizer, while gaining full rights to Elelyso in Brazil. We will continue to manufacture drug substance for Pfizer, subject to certain terms and conditions. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all revenues, globally for Elelyso, excluding Brazil, where we are responsible for all expenses and retain all revenues.

For the first 10-year period after the execution of the Amended Pfizer Agreement, we have agreed to sell drug substance to Pfizer for the production of Elelyso, and Pfizer maintains the right to extend the supply period for up to two additional 30-month periods subject to certain terms and conditions. Any failure to comply with our supply commitments may subject us to substantial financial penalties, which will have a material adverse effect on our business, results of operations and financial condition. The Amended Pfizer Agreement also includes customary

provisions regarding cooperation for regulatory matters, patent enforcement, termination, indemnification and insurance requirements.

On June 18, 2013, we entered into a Supply and Technology Transfer Agreement, or the Brazil Agreement, with Fiocruz, an arm of the Brazilian MoH, for taliglucerase alfa.

In 2017, we received a purchase order from the Brazilian MoH for the purchase of approximately $24.3 million of alfataliglicerase for the treatment of Gaucher patients in Brazil. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in the best interest of our company.

Our Strategy

Our strategy centers around prioritizing existing and new pipeline candidates to focus on products that we believe offer a clear competitive advantage over existing treatments. The strategy was the culmination of an intensive review by our management of our internal resources and of the markets in which we expect we can operate. The following highlights the details of the strategic plan as it relates to our development of an innovative product pipeline using our ProCellEx protein expression system.

Pegunigalsidase alfa (PRX-102) for the Treatment of Fabry Disease. pegunigalsidase alfa, or PRX-102, is designed to be an improved enzyme replacement therapy product for the treatment of Fabry disease given its potential for clinically superior outcomes and enhanced safety when compared to currently marketed enzyme replacement therapies. The product candidate is a key focus for us. We are continuing to enroll patients and recruit clinical sites for our phase III clinical trials of PRX-102, and our phase I/II clinical trial remains ongoing in an extension period.

alidornase alfa (PRX-110) for the Treatment of Cystic Fibrosis. alidornase alfa, our proprietary plant cell recombinant human Deoxyribonuclease 1, is under development for the treatment of cystic fibrosis (CF), to be administered by inhalation. alidornase alfa has an actin inhibition resistance that is designed to improve lung function and lower the incidence of recurrent infections by enhancing the enzyme's efficacy in patients' sputa. We released the final results of our phase II clinical trial of alidornase alfa for the treatment of CF in April 2017. We are currently studying the final results of the trial and are considering different collaboration alternatives as part of our further development plans.

Oral Anti-TNF (OPRX-106) Anti Inflammatory. Oral anti-TNF represents a novel mode of administering a recombinant anti-TNF protein. It is under development as an orally-delivered anti-inflammatory treatment using plant cells as a natural capsule for the expressed protein. Currently, the first 14 patients have completed our phase II proof of concept efficacy study of OPRX-106 for the treatment of ulcerative colitis, and four patients are currently in treatment and follow-up. The trial is evaluating key efficacy endpoints including clinical response and remission utilizing the Mayo score, as well as safety and pharmacokinetics. Interim data generated from the first 14 patients that completed the trial was released in January 2018. We expect to release complete results by the end of March, 2018. Upon review of the final proof of concept data, we intend to identify and collaborate with a well-suited partner for further development.

Potential Pipeline Candidates. We aim to expand our pipeline by leveraging the advantages of our proprietary ProCellEx protein expression technology. The focus is expected to be on biologics with significantly improved clinical profiles than the currently marketed proteins for these indications. Biosimilars will not be a market on which we focus, and will only be considered in the case of proteins that are highly difficult to express or that represent opportunities for early market entry arising from the intellectual property advantages arising from ProCellEx.

Except for the rights to commercialize taliglucerase alfa worldwide (other than Brazil), which we licensed to Pfizer, and the rights to PRX-102 which we licensed to Chiesi for territories outside the United States, we hold the worldwide commercialization rights to all of our proprietary development candidates. We continuously evaluate potential strategic marketing partnerships as well as collaboration programs with biotechnology and pharmaceutical companies and academic research institutes.

ProCellEx: Our Proprietary Protein Expression System

ProCellEx is our proprietary production system. We have developed our ProCellEx system based on our plant cell culture technology for the development, expression and manufacture of recombinant proteins. Our protein expression system does not involve mammalian or animal components or transgenic field-grown, whole plants at any point in the production process. Our ProCellEx system consists of a comprehensive set of capabilities and proprietary technologies, including advanced genetic engineering and plant cell culture technology, which enables us to produce complex, proprietary and biologically equivalent proteins for a variety of human diseases. This protein expression system facilitates the creation and selection of high expressing, genetically stable cell lines capable of expressing recombinant proteins. The entire protein expression process, from initial nucleotide cloning to large-scale production of the protein product, occurs under cGMP-compliant, controlled processes. Our plant cell culture technology uses plant cells, such as carrot and tobacco cells, which undergo advanced genetic engineering and are grown on an industrial scale in a flexible bioreactor system. Cell growth, from scale up through large-scale production, takes place in flexible, sterile, polyethylene bioreactors which are confined to a clean-room environment. Our bioreactors are well-suited for plant cell growth using a simple, inexpensive, chemically-defined growth medium as a catalyst for growth. The reactors are custom-designed and optimized for plant cell cultures, easy to use, entail low initial capital investment, are rapidly scalable at a low cost and require less hands-on maintenance between cycles.

Our ProCellEx system is capable of producing proteins with an amino acid sequence and three dimensional structure practically equivalent to that of the desired human protein, and with a very similar, although not identical, glycan, or sugar, structure, as demonstrated in our internal research and external laboratory studies. In collaboration with the Weizmann Institute of Science, we have demonstrated that the three-dimensional structure of a protein expressed in our proprietary plant cell-based expression system retains the same three-dimensional structure as exhibited by the mammalian cell-based expressed version of the same protein. In addition, proteins produced by our ProCellEx system maintain the biological activity that characterize that of the naturally-produced proteins. Based on these results, we believe that proteins developed using our ProCellEx protein expression system have the intended composition and correct biological activity of their human equivalent proteins.

We believe that our ProCellEx system will enable us to develop recombinant therapeutic proteins yielding substantial cost advantages, accelerated development and other competitive benefits when compared to mammalian cell-based protein expression systems. In addition, our ProCellEx system may enable us, in certain cases, to develop and commercialize recombinant proteins without infringing upon the method-based patents or other intellectual property rights of third parties. The major elements of our ProCellEx system are patent protected in most major countries. Moreover, we expect to enjoy method-based patent protection for the proteins we develop using our proprietary ProCellEx protein expression technology, although there can be no assurance that any such patents will be granted. In some cases, we may be able to obtain patent protection for the compositions of the proteins themselves. We have filed for United States and international composition of matter patents for taliglucerase alfa.

We have successfully demonstrated the feasibility of our ProCellEx system through: (i) the FDA's approval of taliglucerase alfa, and its subsequent approval by other regulatory authorities; (ii) the clinical and preclinical studies we have performed to date, including the positive efficacy and safety data in our clinical trials for taliglucerase alfa, pegunigalsidase alfa, alidornase alfa and OPRX-106 for the treatment of ulcerative colitis; (iii) preclinical results in well-known models in our enzyme for each of Fabry disease, DNase and antiTNF; and (iv) by expressing, on an exploratory, research scale, many additional complex therapeutic proteins belonging to different drug classes, such as enzymes, hormones, monoclonal antibodies, cytokines and vaccines. The therapeutic proteins we have expressed to date in research models have produced the intended composition and similar or superior biological activity compared to their respective human-equivalent proteins. Moreover, several of such proteins demonstrated advantageous biological activity when compared to the biotherapeutics currently available in the market to treat the applicable disease or disorder. We believe that the FDA's approval of taliglucerase alfa represents a strong proof-of-concept of our ProCellEx system and plant cell-based protein expression technology. We also believe that the significant benefits of our ProCellEx system, if further substantiated in clinical trials and in the successful commercialization of taliglucerase alfa and our other product candidates, have the potential to transform the industry standard for the development of complex therapeutic proteins.

Mammalian cell-based expression technology is based on the introduction of a human gene encoding for a specific therapeutic protein into the genome of a mammalian cell, and such systems have become the dominant system for the expression of recombinant proteins due to their capacity for sophisticated, proper protein folding (which is necessary for proteins to carry out their intended biological activity), assembly and post-expression modification, such as glycosilation (the addition of sugar residues to a protein which is necessary to enable specific biological activity by

the protein). Many of the biotechnology industry's largest and most successful therapeutic proteins, including Epogen®, Neupogen®, Cerezyme®, Rituxan®, Humira®, Enbrel®, Neulasta®, Remicade® and Herceptin® are produced through mammalian cell-based expression systems. Mammalian cell-based expression systems can produce proteins with superior quality and efficacy compared to proteins expressed in bacteria and yeast cell-based systems. As a result, the majority of currently approved therapeutic proteins, as well as those under development, are produced in mammalian cell-based systems.

While bacterial and yeast cell-based expression systems were the first protein expression systems developed by the biotechnology industry and remain cost-effective compared to mammalian cell-based production methodologies, proteins expressed in bacterial and yeast cell-based systems lack the capacity for sophisticated protein folding, assembly and post-expression modifications, which are key factors of mammalian cell-based systems. Accordingly, such systems cannot be used to produce glycoproteins or other complex proteins and, therefore, bacterial and yeast cell-based systems are limited to the expression of the most basic, simple proteins, such as insulin and growth hormones.

Several companies and research institutions have been exploring the expression of human proteins in genetically-modified organisms, or GMOs, such as transgenic field-grown, whole plants and transgenic animals. However, these alternate techniques may be restricted by regulatory and environmental risks regarding contamination of agricultural crops and by the difficulty in applying cGMP standards of the pharmaceutical industry to these expression technologies and none of these technologies have been approved by the regulatory agencies with jurisdiction over any substantial market.

To date, our manufacturing facility, in which we utilize our ProCellEx system, was determined to be acceptable by each of the FDA, the European Medicines Agency, or the EMA, ANVISA, the Israeli MOH, the Australian Therapeutic Goods Administration, or the TGA, and Health Canada, after GMP inspections were performed as part of their respective reviews for marketing approval of taliglucerase alfa.

Competitive Advantages of Our ProCellEx Protein Expression System

We intend to continue to leverage the multiple unique advantages of our proprietary ProCellEx protein expression system, including our advanced genetic engineering technology and plant cell-based protein expression methods, to develop our pipeline. Significant advantages of our ProCellEx system over mammalian, bacterial, yeast and transgenic cell-based expression technologies, include the following:

Biologic Optimization. ProCellEx has internal capabilities developed to improve the biologic dynamics of an expressed protein. For example, the proteins produced through our system have uniform glycosilation patterns and therefore do not require the lengthy and expensive post-expression modifications that are required for certain proteins produced by mammalian cell-based systems. Such post-expression modifications in mammalian cell-produced proteins are made in order to expose the terminal mannose sugar residues, which are structures on a protein that are key elements in allowing the expressed protein to bind to a target cell and subsequently be taken into the target cell for therapeutic benefit. In addition, these steps do not guarantee the exposure of all of the required terminal mannose sugar residues, resulting in potentially lower effective yields and inconsistency in potency from batch to batch. We believe this quality increases the potency and consistency of the expressed proteins, and thus, the effectiveness of the protein which presents an additional cost advantage of ProCellEx over competing protein expression methodologies.

Ability to Penetrate Certain Patent-Protected Markets. ProCellEx has the potential to provide workaround manufacturing that does not infringe the method-based patents or other intellectual property rights of third parties. Certain biotherapeutic proteins available for commercial sale are not protected by patents that cover the compound and are available for use in the public domain. Rather, the process of expressing the protein product in mammalian or bacterial cell systems is protected by method-based patents. Using our plant cell-based protein expression technology, we are able to express an equivalent protein without infringing upon these method-based patents. Moreover, we expect to enjoy method-based patent protection for the proteins we develop using our ProCellEx system, although

there can be no assurance that any such patents will be granted. In some cases, we may be able to obtain patent protection for the compositions of the proteins themselves. We have filed for U.S. and international composition of matter patents for PRX-102 and certain of our other product candidates.

Broad Range of Expression Capabilities. ProCellEx is able to produce a broad array of complex glycosilated proteins, which are difficult to produce in other systems, such as bacterial and yeast cell-based systems, as well as CHO systems. We have successfully demonstrated the feasibility of our ProCellEx system by producing, on an exploratory, research scale, a variety of therapeutic proteins belonging to different classes of recombinant drugs, such as enzymes, hormones, monoclonal antibodies, cytokines and vaccines. We have demonstrated that the recombinant proteins we have expressed to date have the intended composition and correct biological activity of their human-equivalent protein, with several of such proteins demonstrating advantageous biological activity compared to the currently available biotherapeutics. In specific cases, we have been successful in expressing proteins that have not been successfully expressed in other production systems.

Significantly Lower Capital and Production Costs. ProCellEx entails a lower cost of scale-up and of production. Plant cells grow rapidly under a variety of conditions and are not as sensitive as mammalian cells are to temperature, pH and oxygen levels which generally can only be grown under near perfect conditions. Our system, therefore, does not require the highly complex, expensive, stainless steel bioreactors typically used in mammalian cell-based production systems to maintain very specific temperature, pH and oxygen levels. Instead, we use simple polyethylene bioreactors that can be maintained at the room temperature of the clean-room in which they are placed. This system also reduces ongoing production and monitoring costs typically associated with mammalian cell-based expression technologies. Furthermore, while mammalian cell-based systems require very costly growth media at various stages of the production process to achieve target yields of proteins, plant cells require only simple and much less expensive solutions based on sugar, water and microelements at infrequent intervals to achieve target yields. Mammalian cell-based expression systems require large quantities of sophisticated and expensive growth medium to accelerate the expression process.

Elimination of the Risk of Viral Transmission or Infection by Mammalian Components. By nature, plant cells do not carry the risk of infection by human or other animal viruses. Mammalian cells, to the contrary, are susceptible to viral infections, including human viruses, and several cases of viral contamination have occurred. As a result, the risk of contamination of our products under development and the potential risk of viral transmission from our product and product candidates to future patients, whether from known or unknown mammalian viruses, is eliminated. Because our products and product candidates do not bear the risk of mammalian viral transmission, we are not required by the FDA or other regulatory authorities to perform the constant monitoring procedures for mammalian viruses during the protein expression process that are required in mammalian cell-based production. In addition, the production process of our ProCellEx system is void of any mammalian components which are susceptible to the transmission of prions, such as those related to bovine spongiform encephalopathy (commonly known as “mad-cow disease”). These factors further reduce the risks and operating costs of ProCellEx compared to mammalian cell-based expression systems.

The FDA and other regulatory authorities require viral inactivation and other rigorous and detailed procedures for mammalian cell-based manufacturing processes in order to address these potential hazards, thereby increasing the cost and time demands of such expression systems. Furthermore, the current FDA and other procedures only ensure screening for scientifically identified, known viruses. Accordingly, compliance with current FDA and other procedures does not fully guarantee that patients are protected against transmission of unknown or new potentially fatal viruses that may infect mammalian cells.

Potential ability to administer active therapeutic proteins orally. We are using ProCellEx to produce active recombinant proteins through oral administration of plant cells expressing biotherapeutic proteins. In such method, an enzyme is naturally encapsulated within plant cells genetically engineered to express the targeted enzyme. Plant cells have the unique attribute of a cellulose cell wall which makes them resistant to enzyme degradation when passing through the digestive tract. The plant cell itself serves as a delivery vehicle, once released and absorbed, to transport an enzyme in active form to the bloodstream. If proven effective, this would be the first time an enzyme will be administered orally rather than through intravenous therapy. To date we have completed successful preclinical animal studies for oral GCD and oral antiTNF, and early clinical trials of oral GCD in Gaucher patients. In addition, we have completed a phase IIa proof of concept trial of oral antiTNF as well as a phase I clinical trial of oral antiTNF in healthy volunteers.

Our First Commercial Product – Elelyso for the Treatment of Gaucher Disease

Elelyso (taliglucerase alfa), our first commercial product, is a plant cell expressed recombinant glucocerebrosidase enzyme (GCD) for the treatment of Gaucher disease. On May 1, 2012, the FDA approved Elelyso for injection as an enzyme replacement therapy (ERT) for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease. It was subsequently approved by the Israeli MOH, ANVISA and the regulatory authorities of other countries. In August 2014, the FDA approved Elelyso for injection for pediatric patients, and other jurisdictions, including Brazil, approved pediatric indications thereafter.

Gaucher disease, a hereditary, genetic disorder with severe and debilitating symptoms, is the most prevalent lysosomal storage disorder in humans. Lysosomal storage disorders are metabolic disorders in which a lysosomal enzyme, a protein that degrades cellular substrates in the lysosomes of cells, is mutated or deficient. Lysosomes are small membrane-bound cellular structures within cells that contain enzymes necessary for intracellular digestion. Gaucher disease is caused by mutations or deficiencies in the gene encoding GCD, a lysosomal enzyme that catalyzes the degradation of the fatty substrate, glucosylceramide (GlcCer). Patients with Gaucher disease lack or otherwise have dysfunctional GCD and, accordingly, are not able to break down GlcCer. The GlcCer accumulates in lysosomes of certain white blood cells called macrophages which consequently become highly enlarged. The enlarged cells accumulate in the spleen, liver, lungs, bone marrow and brain. Signs and symptoms of Gaucher disease may include enlarged liver and spleen, abnormally low levels of red blood cells and platelets and skeletal complications. In some cases, the patient may suffer an impairment of the central nervous system.

The standard of care for Gaucher disease is enzyme replacement therapy using recombinant GCD to replace the mutated or deficient natural GCD enzyme. Enzyme replacement therapy is a medical treatment in which recombinant enzymes are injected into patients in whom the enzyme is lacking or dysfunctional. Cerezyme® and VPRIV® are the only other ERTs currently available for the treatment of Gaucher disease. In addition, Cerdelga® (eliglustat) is a substrate reduction therapy for Gaucher disease that was approved for marketing by the FDA in August 2014 and by the European Commission in January 2015. Finally, Zavesca (miglustat) is a small molecule drug for the treatment of Gaucher disease. Zavesca has been approved by the FDA for use in the United States as an oral treatment. However, it has many side effects and the FDA has approved it only for administration to those patients who cannot be treated through ERT, and, accordingly, have no other treatment alternative. As a result, the use of Zavesca has been limited with respect to the treatment of Gaucher disease. However, Zavesca is also used to treat other rare disorders.

We have licensed to Pfizer the worldwide rights to Elelyso with the exception of Brazil, a market where we have retained own full rights.

Our Pipeline Drug Candidates

PRX-102 for the Treatment of Fabry Disease

We are developing PRX-102, our proprietary plant cell expressed chemically modified version of the recombinant alpha-GAL-A protein, a therapeutic enzyme, for the treatment of Fabry disease, a rare genetic lysosomal storage disorder. We believe that PRX-102 has the potential to be a significantly improved version of the currently marketed Fabry disease enzymes, Fabrazyme® and Replagal®, with improved activity in the Fabry disease target organs and significantly longer half-life due to higher stability, which together can potentially lead to improved substrate clearance and significantly lower formation of antibodies, as observed in our phase I/II clinical trial in Fabry patients. We believe that the treatment of Fabry disease is a specialty clinical niche with the potential for high growth as there is a significant unmet medical need for Fabry disease treatments.

Fabry Disease Background

Fabry disease is a serious, life-threatening condition. It is a disease or condition associated with morbidity that has a substantial impact on survival, day-to-day function, and the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. Fabry disease is an X-linked multisystem lysosomal storage disorder caused by the absence or reduction of -galactosidase-A (-Gal-A) activity, which is a lysosomal enzyme that catalyzes the hydrolysis of globotriaosylceramide (Gb3) from oligosaccharides, glycoproteins and glycolipids. The absence or reduction of this enzymatic activity leads to the progressive accumulation of glycolipids, especially Gb3, in

capillary endothelial cells, podocytes, tubular cells, glomerular endothelial cells, mesangial cells, interstitial cells, cardiomyocytes, fibroblasts, and neurons. The accumulation of glycosphingolipids (e.g., Gb3) leads to chronic pain, skin lesions, cardiac, deficiencies, and, in particular, renal involvement. End-stage renal failure and cardiomyopathy often lead to early death in Fabry patients. Fabry disease causes substantial reduction in life-expectancy, by an average of 15 years in female patients and 20 years in male patients, compared to the general population.

Current Treatments of Fabry Disease

Currently there are two enzyme replacement therapies drugs available on the market to treat Fabry disease. Fabrazyme, marketed by Genzyme Corporation (acquired by Sanofi), is approved for the treatment of Fabry disease in the United States and the European Union. Sanofi reported €722 million (approximately $865 million) in worldwide sales of Fabrazyme in 2017. The other approved enzyme replacement therapy for the treatment of Fabry disease in the European Union is Replagal, which is marketed by Shire. Shire reported $472 million in sales of Replagal in 2017. In April 2016, Galafold™, a chaperone therapy manufactured by Amicus Therapeutics, Inc., or Amicus, was approved in the European Union as a monotherapy for Fabry disease in patients with amenable mutations. Galafold has also been accepted for marketing in a number of other countries. Amicus reported revenues of approximately $36 million in sales of Galafold in 2017.

PRX-102 Development Program

In October 2016, the first patient was dosed in our global phase III clinical trial of PRX-102 for the treatment of Fabry disease. Over 40 sites are currently participating in this trial. The phase III efficacy and safety clinical trial, which we refer to as the BALANCE Study, is a multi-center, randomized, double-blind, active control study of PRX-102 in Fabry patients with impaired renal function. The trial is designed to enroll 78 patients previously treated with Fabrazyme (agalsidase beta) with a stable dose for at least six months. Enrolled patients are randomized to continue treatment with 1 mg/kg of either Fabrazyme or PRX-102, at a 2:1 ratio of PRX-102 to Fabrazyme, respectively. Patients are to be treated via intravenous (IV) infusions every two weeks. The sites are recruiting adult symptomatic Fabry patients with plasma and/or leucocyte alpha galactosidase activity (by activity assay) less than 30% mean normal levels. All patients must have had treatment with a dose of 1 mg/kg agalsidase beta per infusion every two weeks for at least one year. In addition, to be included in the trial, patients need to have certain eGFR values and a meaningful decline in annualize eGFR slope.

The primary endpoint for the BALANCE study, which was agreed with both the FDA and the EMA, is the comparison in the rate of decline of eGFR slope between Fabrazyme and PRX-102. At 12 months, we intend to conduct an interim analysis to test for non-inferiority to support an anticipated regulatory filing with the EMA. At the same time, we intend to approach the FDA to request its review of the then totality of data. Notwithstanding, patients enrolled in the study will continue to be treated for a total of 24 months, at which point the data will be analyzed to test for superiority, which is the original guidance we received from the FDA.

Concurrently with the BALANCE study, we are also performing a supportive phase III clinical trial of PRX-102, which we refer to as the BRIDGE Study. The BRIDGE study is an open-label, single-arm, switchover study to assess the efficacy and safety of PRX-102 in Fabry patients currently treated with Replagal. The trial is designed to enroll 22 patients. The objective of the study is to generate safety and efficacy data of patients switched from Replagal to PRX-102 over a 12-month period. The endpoints of the study are safety, mean annualized change (slope) in eGFR, pain, plasma lyso GB3, immunogenicity and Quality of Life.

In addition to the BALANCE and BRIDGE studies, we are performing a third clinical trial to evaluate the safety and efficacy of administering 2 mg/kg of PRX-102 once monthly in Fabry patients. PRX-102 with a 2 mg/kg dose was found to be safe and well tolerated with no formation of antibodies in our phase I/II clinical trial of PRX-102 for the treatment of Fabry disease. Additionally, in our phase I/II clinical trial, 2 mg/kg of PRX-102 demonstrated approximately a 40 times higher circulatory half-life compared with other enzyme replacement therapies, and, as demonstrated in a Fabry mice model, with materially higher active enzyme reaching target organs affected by Fabry disease. Pharmacokinetic (PK) analysis and modeling from the phase I/II clinical trial indicate that PRX-102 levels at the second week after infusion remain 10 times higher than published Fabrazyme levels at the day of infusion. Moreover, the amount of PRX-102 in the circulation at weeks three and four, are higher than those of Fabrazyme during the two-week treatments. These results provide strong rationale for the clinical evaluation of a once-monthly dosing.

We plan to enroll up to 30 Fabry patients currently treated with an approved enzyme replacement therapy in this study. A safety and efficacy evaluation will occur at 12 months with additional long term follow-up.

Phase I/II Clinical Data

Our phase I/II clinical trial of PRX-102, which we completed in 2015, was a worldwide, multi-center, open label, dose ranging study to evaluate the safety, tolerability, pharmacokinetics, immunogenicity and efficacy parameters of PRX-102 in adult Fabry patients. Sixteen adult naive Fabry patients (9 male and 7 female) completed the trial, each in one of three dosing groups, 0.2 mg/kg, 1mg/kg and 2mg/kg. Each patient received intravenous infusions of PRX-102 every two weeks for 12 weeks, with efficacy follow-up after six-month and twelve-month periods. All patients that completed the trial opted to continue to receive 1 mg/kg of PRX-102 in an open-label, 60-month extension study under which all patients have been switched to receive 1 mg/kg of the drug, the selected dose for our phase III studies of PRX-102.

The data set forth below was recorded at 24 months from 11 patients enrolled and treated in the long-term open-label extension trial. Patients who did not continue in the extension trial included female patients who became or planned to become pregnant, and therefore were unable to continue in accordance with the study protocol, and patients that relocated to a location where treatment was not available under the clinical study.

Efficacy

- Lyso Gb3 levels decreased approximately 90% from baseline (see Figure 1);
- Renal function remained stable with mean eGRF levels of 108.02 and 107.20 at baseline and 24 months, respectively with a modest annual eGFR slope of -2.1; (see Figure 2)
- An improvement across all the gastrointestinal symptoms evaluated, including severity and frequency of abdominal pain and frequency of diarrhea, were noted (see Figure 1);
- Cardiac parameters, including LVM, LVMI and EF, remained stable with no cardiac fibrosis development detected;
- In conclusion, an improvement of over 40% in disease severity was shown as measured by the Mainz Severity Score Index (MSSI), a score compiling the different elements of the disease severity including neurological, renal and cardiovascular parameters; and
- An improvement was noted in each of the individual parameters of the MSSI.

Figure 1. Continuous reductions observed over 24 months

Figure 2. Continuous clinical stability observed over 24 months

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Safety

- The majority of adverse events were mild to moderate in severity, and transient in nature;

- During the first 12 months of treatment, only three of 16 patients (less than 19%) formed anti-drug antibodies (ADA), of which two of these patients (less than 13%) had neutralizing antibodies;

- Importantly, however, the ADAs turned negative for all three of these patients following 12 months of treatment; and

- The ADA positivity effect had no observed impact on the safety, efficacy or continuous biomarker reduction of PRX-102.

alidornase Alfa (PRX-110) for the Treatment of Cystic Fibrosis

alidornase alfa is our proprietary plant cell recombinant form of human deoxyribonuclease I (DNase I) that we are developing for the treatment of CF, to be administered by inhalation. DNase I cleaves extracellular DNA and thins the thick mucus that accumulates in the lungs of CF patients. Currently, Pulmozyme® is the only DNase I commercially available, with annual sales of approximately CHF 730 million (approximately $748 million) in sales for 2017 according to public reports by F. Hoffman-La Roche Ltd.

In vitro studies with PRX-110 demonstrated improved enzyme kinetics, significantly reduced sensitivity to inhibition by actin and improved ex vivo efficacy when compared to Pulmozyme. Preclinical studies of alidornase alfa administered by inhalation showed substantial enzymatic activity in lungs.

We designed alidornase alfa, through chemical modification, to be resistant to inhibition by actin so as to improve lung function and lower the incidence of recurrent infections by enhancing the enzyme's efficacy in patients' sputa. Actin, a potent inhibitor of DNase, is found in high concentration in CF patients' sputum. As demonstrated in Figure 3, the activity of alidornase alfa, as demonstrated in in vitro studies, remains almost with no change in the relevant actin concentration found in CF patients while Pulmozyme is degraded significantly.

Figure 3. Actin and DNase concentrations in human sputum tested in *in vitro* assays; Rheology Data Analysis in in human sputum samples

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In addition, alidornase alfa has demonstrated improved disease parameters in human models sputum testing when compared to the currently marketed product. In particular, alidornase alfa has demonstrated a reduction in mucus viscosity in human sputum samples when compared to the currently marketed product. See Figure 3.

alidornase alfa Development Program

We completed a phase I clinical trial of alidornase alfa with 18 healthy volunteers in which alidornase alfa was found to be safe and tolerable.

In July 2016 we commenced a phase IIa clinical trial of alidornase alfa for the treatment of CF, and we released the final results of the study in April 2017. Sixteen patients were enrolled in the study, all of whom completed the study. The phase II trial was a 28-day switchover study to evaluate the safety and efficacy of alidornase alfa in CF patients previously treated with Pulmozyme (currently the only commercially available DNase therapy). Participation in the trial was preceded by a two-week washout period from Pulmozyme before treatment with alidornase alfa via inhalation.

The primary efficacy results show that treatment with alidornase alfa resulted in clinically meaningful lung function improvement, as demonstrated by a mean absolute increase in the percent predicted forced expiratory volume in one second (ppFEV1) of 3.4 points from baseline. Moreover, a mean absolute increase in ppFEV1 of 2.8 points was also observed in patients participating in the trial when compared to measurements taken from patients at initiation before the switch from Pulmozyme to alidornase alfa. See Figure 4.

Figure 4. Phase II trial demonstrates clinically meaningful lung function improvement

A commercially available small molecule CFTR modulator for the treatment of CF has reported a mean absolute increase in ppFEV1 of 2.5 from baseline in its registration clinical study. This score was achieved while 74% of the patients participating in the trial of the CFTR modulator were also treated with the modulator on top of Pulmozyme. While this marketed CFTR addresses a certain mutation applicable to less than 50% of CF patients, alidornase alfa is being developed to treat all CF patients.

Sputa available DNA samples were analyzed for approximately half of the patients. A mean reduction of over 70% in DNA content from baseline was observed, and a mean reduction of over 90% from baseline was observed for sputa visco-elasticity. Correlation between improvement in sputa parameters and pulmonary function was observed. See Figure 5.

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Figure 5. Decrease in sputum DNA content and sputum viscosity upon alidornase alfa treatment initiation

In addition, an in vitro study of alidornase alfa demonstrated a significant inhibition of Pseudomonas Aeruginosa, with alidornase alfa treated colonies reduced by over 50%, compared to baseline. Pseudomonas, strains of bacteria that are widely found in the environment, are a major cause of lung infections in CF patients. Chronic pulmonary infection is a leading cause of morbidity and mortality in CF patients, despite the aggressive use of antibiotics, and Pseudomonas is the most prevalent organism in the airway colonization of CF patients.

PK analysis performed indicated alidornase alfa is not absorbed into a patient's circulatory system, suggesting higher levels of alidornase alfa remains available in the patient's lungs. This provides further support for the potential that alidornase alfa may offer additional efficacy to CF patients.

The above-mentioned material decrease in visco-elasticity and DNA presence in CF patients' sputa, coupled with the significant inhibition of Pseudomonas and higher levels of alidornase alfa available in the patients' lungs, provides further supportive evidence of improved lung function after treatment with alidornase alfa, as demonstrated by the increase in FEV1.

alidornase alfa was well tolerated with no serious adverse events reported.

OPRX-106; Oral antiTNF for the treatment of inflammatory diseases

OPRX-106, our oral antiTNF product candidate, is a recombinant antiTNF (Tumor, Necrosis Factor) protein that we are expressing through ProCellEx. Auto-immune-mediated inflammatory disorders are conditions that are characterized by common pathways that lead to inflammation and are caused or triggered by a compromised or dysregulation of the normal immune response. Immune-mediated inflammatory disorders can cause organ damage, and are associated with increased morbidity. Common auto-immune diseases include rheumatoid arthritis, inflammatory bowel disease (IBD) such as ulcerative colitis and crohn's disease, psoriasis, and others. Some of the major treatments are antiTNF drugs, administered as subcutaneous injections or as intravenous infusions. Sales of anti-TNF drugs exceeded $30 billion annually. Well-known antiTNF drugs include Humira, Remicade and Enbrel.

OPRX-106 is a plant cell-expressed form of the fused protein that is naturally encapsulated within BY-2 cells genetically engineered to express the enzyme. Plant cells have the unique attribute of a cellulose cell wall which makes them resistant to enzyme degradation when passing through the digestive tract. The plant cell itself serves as a delivery vehicle, once released and absorbed, to transport the enzyme in active form to the bloodstream. If proven effective, our experimental oral antiTNF would be the first protein to be administered orally rather than through injection. We believe that our oral delivery mechanism could be applied to additional proteins and has the potential to change the method of protein administration in certain indications.

OPRX-106 Development Program

OPRX-102 for the treatment of ulcerative colitis is currently the subject of a phase IIa clinical trial. The first patient was enrolled in the trial in November 2016. The phase II clinical trial is a randomized, open label, 2-arm study of OPRX-106 in patients with active mild to moderate ulcerative colitis. A total of 24 patients were enrolled and randomized to receive 2 mg or 8 mg of OPRX-106, administered orally, once daily, for 8 weeks. Currently, the first 14 patients have completed the study, and four patients are currently in treatment and follow-up. The trial evaluated key efficacy endpoints including clinical response and remission utilizing the Mayo score, as well as safety and pharmacokinetics. Interim data generated from the first 14 patients that completed the trial was released in January 2018. The interim data demonstrates that 57% of the patients achieved clinical response and 36% achieved clinical remission at week 8. In the rectal bleeding analysis, a sub category of the Mayo score, 79% of those patients show an improvement. In addition, the majority of those patients show improvement in the study's additional efficacy endpoints, with 86% of the patients achieved an improvement in calprotectin, a protein biomarker present in the feces indicating intestinal inflammation, and 64% have an improved Geboes score, a histopathological scoring for the assessment of disease activity in ulcerative colitis. We except to release complete results by the end of March, 2018.

For purposes of the study, clinical response at week 8 is defined as a decrease in the Mayo score of at least 3 points and either a decrease in the sub-score for rectal bleeding of at least 1 point from baseline, or rectal bleeding sub-score of 0 or 1. Clinical remission at week 8 is defined as clinically symptom free, a Mayo score ≤ 2, with no individual sub-score exceeding 1 point after treatment.

Treatment was well tolerated and the majority of adverse events have been mild to moderate and transient in nature, with headaches being the most common. No immunosuppression was evident.

The results from our phase I clinical trial of OPRX-106 demonstrated that the drug was safe and well tolerated, and showed biological activity in the gut. The phase I clinical trial was a randomized, parallel-design, open-label study designed to evaluate the safety and pharmacokinetics of OPRX-106 in healthy volunteers. The trial enrolled 14 subjects that were randomized to one of three dosing cohorts receiving OPRX-106 doses equivalent to 2mg, 8mg or 16mg Tumor Necrosis Factor receptor-Fc fusion protein. Subjects received once daily oral administrations for five consecutive days. The results demonstrated that oral administration of OPRX-106 is safe and well tolerated. No major side effects were noted, and no suppression of the immune system was observed. Regulatory T cell activation showing biological activity in the gut was observed. Fluorescence-activated cell sorting analysis (FACS) was performed using various antibodies for surface markers, and it was observed that all three dosages of OPRX-106 promoted the induction of various subsets of T cells, some of which are correlated with anti-inflammatory response.

Commercialization Agreement with Chiesi Farmaceutici

On October 19, 2017, Protalix Ltd. and Chiesi entered into the Chiesi Agreement pursuant to which Chiesi was granted an exclusive, license for all markets outside of the United States to develop and commercialize pegunigalsidase alfa. Protalix Ltd. retained the right to commercialize pegunigalsidase alfa in the United States. Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to $25 million in development costs, capped at $10 million per year. Protalix Ltd. is also eligible to receive an additional up to $320 million, in the aggregate, in regulatory and commercial milestone payments. Protalix Ltd. and Chiesi have agreed to a specific allocation of the responsibilities for the continued development efforts for pegunigalsidase alfa. Protalix Ltd. agreed to manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi is required to make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa. The Chiesi Agreement also provides for reimbursement by Chiesi of certain costs to be incurred by Protalix Ltd.

We are required to pay a royalty equal to 3% of the PRX-102-related revenues Chiesi records under the Chiesi Agreement to the National Authority for Technological Innovation, or NATI.

Technology Transfer Agreement with Fiocruz

Our Brazil Agreement became effective in January 2014. The technology transfer is designed to be completed in four stages and is intended to transfer to Fiocruz the capacity and skills required for the Brazilian government to construct its own manufacturing facility, at its sole expense, and to produce a sustainable, high-quality, and cost-effective supply of taliglucerase alfa. The initial term of the technology transfer is seven years. The agreement contains certain purchase commitments by Fiocruz. If Fiocruz fails to comply with the purchase commitments, we may terminate the agreement, and all of our rights to the technology will be returned.

In 2017, we received a purchase order from the Brazilian MoH for the purchase of approximately $24.3 million of alfataliglicerase for the treatment of Gaucher patients in Brazil. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in the best interest of our company.

The Brazil Agreement may be extended for an additional five-year term, as needed, to complete the technology transfer. All of the terms of the arrangement, including the minimum annual purchases, will apply during the additional term. Upon completion of the technology transfer, and subject to Fiocruz receiving approval from ANVISA to manufacture taliglucerase alfa in its facility in Brazil, the agreement will enter into the final term and will remain in effect until our last patent in Brazil expires. During such period, Fiocruz will be the sole provider of this important treatment option for Gaucher patients in Brazil and shall pay us a single-digit royalty on net sales.

Intellectual Property

We maintain a proactive intellectual property strategy which includes patent filings in multiple jurisdictions, including the United States and other commercially significant markets. As of December 31, 2017, we held, or had license rights to, 69 patents and 58 pending patent applications with respect to various compositions, methods of production and methods of use relating to our ProCellEx protein expression system and our proprietary product pipeline. Of the above, one is a joint patent, eight are joint patent applications, and one is a licensed patent application.

Our competitive position and future success depend in part on our ability, and that of our licensees, to obtain and leverage the intellectual property covering our product candidates, know-how, methods, processes and other

technologies, to protect our trade secrets, to prevent others from using our intellectual property and to operate without infringing the intellectual property of third parties. We seek to protect our competitive position by filing United States, European Union, Israeli and other foreign patent applications covering our technology, including both new technology and improvements to existing technology. Our patent strategy includes obtaining patents, where possible, on methods of production, compositions of matter and methods of use. We also rely on know-how, continuing technological innovation, licensing and partnership opportunities to develop and maintain our competitive position.

We issued a series of 7.5% convertible notes in December 2016 and July 2017, which are guaranteed by our subsidiaries and secured by perfected liens on all of our material assets, primarily consisting of our intellectual property assets, including a stock pledge of our foreign subsidiaries in favor of the holders of outstanding 7.5% convertible notes.

As of December 31, 2017, our patent portfolio consisted of several patent families (consisting of patents and/or patent applications) covering our technology, protein expression methodologies and system and product candidates, as follows:

- With respect to our ProCellEx protein expression system, we held nine issued patents and seven patent applications relating to the large scale production of proteins in cultured plant cells. The issued patents and any patents to issue in the future based on pending patent applications in this patent family, if at all, are expected to expire in 2028. One patent relating to a separate family, covering methods for culturing and harvesting plant cells and/or tissues in consecutive cycles is expected to expire in 2025.

- We held a patent family containing 24 issued patents and one patent application in India, South Africa, Russian Federation, Australia, China, the United States, Ukraine, Singapore, Japan, Europe, Hong Kong, Mexico, Korea, Canada, Brazil and Israel relating to the production of recombinant glycosylated lysosomal proteins in our plant culture platform, including taliglucerase alfa, and uses of these proteins and cells containing these proteins for the treatment of lysosomal disorders. The issued patents and any patents to issue in the future based on pending patent applications in this patent family, if at all, are expected to expire in 2024.

- We held a patent family containing three granted patents relating to a system and method for production of antibodies in a plant cell culture, and antibodies produced in such a system. The issued patents in this patent family are expected to expire in 2025.

- We held a patent family containing four issued patents in Europe, South Africa, Australia and Israel, and one pending patent application relating to a new method for delivering active recombinant proteins systemically through oral administration of transgenic plant cells. The issued patents and any patents to issue in the future based on patent applications in this patent family, if at all, are expected to expire in 2026.

- We held a patent family containing five granted patents in the United States, Europe, South Africa, Israel and Australia, relating to saccharide containing protein conjugates. The issued patents and any patents to issue in the future based on the patent applications in this patent family, if at all, are expected to expire in 2028.

- We held a patent family containing four granted patents in Japan, United States, Europe and China, and six pending patent applications relating to Nucleic Acid construct for expression of alpha-galactosidase enzyme in plants and plant cells. The patents to issue in the future based on the patent applications in this patent family, if at all, are expected to expire in 2031.

- We held a patent family containing 16 granted patents in Europe, United States, Australia, Japan, Russian Federation, China, Hong Kong, Singapore, New Zealand and South Africa, and eight pending patent applications relating to multimeric protein structures of -galactosidase and to uses thereof in treating Fabry disease. The issued patents and any patents to issue in the future based on the patent applications in this patent family, if at all, are expected to expire in 2031.

- We held three patent families containing two granted patents in the United States and six pending applications relating to plant recombinant human DNase I and uses in therapy. The patents to issue in the future based on these patent applications, if at all, are expected to expire in 2033.

- We held a a patent family containing 11 patent applications relating to chemically modified plant recombinant human DNase I and uses in therapy. The patents to issue in the future based on this patent application, if at all, are expected to expire in 2036.

- We held three families containing 10 patent applications relating to plant recombinant TNF alpha inhibitor polypeptides. The patents to issue in the future based on these patent applications, if at all, are expected to expire in 2034/2035.

- Our patent portfolio includes a patent that we co-own that covers human glycoprotein hormone and chain splice variants, including isolated nucleic acids encoding these variants. More specifically, this patent covers a new splice variant of human FSH. This patent was issued in the United States and is expected to expire in 2024.

- We co-own and have an exclusive license to a patent family, containing eight pending applications, that covers use of plant cells expressing a TNF alpha polypeptide inhibitor in therapy. The patents to issue in the future based on these patent applications, if at all, are expected to expire in 2034.

- We have licensed the rights to a United States patent application covering oral composition comprising a TNF antagonist. The patents to issue in the future based on this application, if at all, are expected to expire in 2034.

We are aware of U.S. patents, and corresponding international counterparts of such patents, owned by third parties that contain claims covering methods of producing GCD. We do not believe that, if any claim of infringement were to be asserted against us based upon such patents, taliglucerase alfa would be found to infringe any valid claim under such patents. However, there can be no assurance that a court would find in our favor or that, if we choose or are required to seek a license to any one or more of such patents, a license would be available to us on acceptable terms or at all.

In April 2005, Protalix Ltd. entered into a license agreement with Icon Genetics AG, or Icon, pursuant to which we received an exclusive worldwide license to develop, test, use and commercialize Icon's technology to express certain proteins in our ProCellEx protein expression system. We are also entitled to a non-exclusive worldwide license to make and have made other proteins expressed by using Icon's technology in our technology. As consideration for the license, we are obligated to make royalty payments equal to varying low, single-digit percentages of net sales of products by us, our affiliates, or any sublicensees under the agreement. In addition, we are obligated to make milestone payments equal to $350,000, in the aggregate, for each product developed under the license, upon the achievement of certain milestones.

Our license agreement with Icon remains in effect until the earlier of the expiration of the last patent under the agreement or, if all of the patents under the agreement expire, 20 years after the first commercial sale of any product under the agreement. Icon may terminate the agreement upon written notice to us that we are in material breach of our obligations under the agreement and we are unable to remedy such material breach within 30 days after we receive such notice. Further, Icon may terminate the agreement in connection with certain events relating to a wind up or bankruptcy, if we make a general assignment for the benefit of our creditors, or if we cease to conduct operations for a certain period. Icon may also terminate the exclusivity granted to us by written notice if we fail to reach certain milestones within a designated period of time. Notwithstanding the termination date of the agreement, our obligation to pay royalties to Icon under the agreement may expire prior to the termination of the agreement, subject to certain conditions.

Manufacturing

We use our current facility, which has approximately 20,000 sq/ft of clean rooms built according to industry standards, to develop, process and manufacture pegunigalsidase alfa, taliglucerase alfa and other recombinant proteins. Pegunigalsidase alfa and our other drug product candidates, as well as taliglucerase alfa, must be manufactured in a sterile environment and in compliance with cGMPs set by the FDA and other relevant foreign regulatory authorities. We are currently producing Fabry drug substance for our phase III and other clinical trials, as well as the manufacture of the taliglucerase alfa we need in the near future, included the taliglucerase alfa to be purchased by Pfizer under the Pfizer Agreement. In addition, we intend to use our manufacturing space to produce all of the drug substance needed in connection with the clinical trials for our product candidates.

In 2017, the FDA approved the Supplemental New Drug Application (sNDA) we submitted to allow us to convert our manufacturing facility from a single dedicated product facility to a multi-product facility. We expect that the conversion will allow us to realize potentially significant operational savings. Our facility's current capacity can serve all of our current and expected commercial and clinical needs, and we believe it will be sufficient to serve our production needs for the anticipated commercialization of PRX-102.

Our manufacturing facilities in Carmiel, Israel, have undergone successful audits by the Israeli MOH, the FDA, ANVISA, and the European Union under the European Union's centralized marketing authorization procedure, the Australian TGA and Health Canada.

Our current facility in Israel has been granted "Approved Enterprise" status, and we have elected to participate in the alternative benefits program. Our facility is located in a Zone A location, and, therefore, our income from the Approved Enterprise will be tax exempt in Israel for a 10-year period commencing with the year in which we first generate taxable income from the relevant Approved Enterprise and after we use our net operating loss carryforwards, or "NOLs." We expect to be entitled to similar tax benefits for a number of years thereafter. To remain eligible for these tax benefits, we must continue to meet certain conditions, and if we increase our activities outside of Israel, for example, by future acquisitions, such increased activities generally may not be eligible for inclusion in Israeli tax benefit programs. In addition, our technology is subject to certain restrictions with respect to the transfer of technology and manufacturing rights. "See Risk Factors—The manufacture of our products is an exacting and complex process, and if we or one of our materials suppliers encounter problems manufacturing our products, it will have a material adverse effect on our business and results of operations."

Raw Materials and Suppliers

We believe that the raw materials that we require throughout the manufacturing process of Elelyso, PRX-102, alidornase alfa and OPRX-106 and our other current and potential drug product candidates are widely available from numerous suppliers and are generally considered to be generic industrial biological supplies. We rely on a single approved supplier for certain materials relating to the current expression of our proprietary biotherapeutic proteins through ProCellEx. We have identified additional suppliers for most of the materials required for the production of our product candidates.

Development and regulatory approval of our pharmaceutical products are dependent upon our ability to procure active ingredients and certain packaging materials from sources approved by the FDA and other regulatory authorities. Since the FDA and other regulatory approval processes require manufacturers to specify their proposed suppliers of active ingredients and certain packaging materials in their applications, FDA approval of a supplemental application to use a new supplier in connection with any drug candidate or approved product, if any, would be required if active ingredients or such packaging materials were no longer available from the specified supplier, which could result in manufacturing delays. From time to time, we intend to continue to identify alternative FDA-approved suppliers to ensure the continued supply of necessary raw materials.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly evolving technology and significant competition. Competition from numerous existing companies and others entering the fields in which we operate is intense and expected to increase. Most of these companies have substantially greater research and development, manufacturing, marketing, financial, technological personnel and managerial resources than we do. In addition, many specialized biotechnology companies have formed collaborations with large, established companies to support

research, development and commercialization of products that may be competitive with our current and future product candidates and technologies. Acquisitions of competing companies by large pharmaceutical or biotechnology companies could further enhance such competitors' financial, marketing and other resources. Academic institutions, governmental agencies and other public and private research organizations are also conducting research activities and seeking patent protection and may commercialize competitive products or technologies on their own or through collaborations with pharmaceutical and biotechnology companies.

There are two approved ERTs for the treatment of Fabry disease; Fabrazyme which is marketed by Genzyme and Replagal, which is marketed by Shire. Fabrazyme is available in the United States and the European Union. Replagal is available in the European Union and certain other territories outside the United States. In addition, we are aware of other late clinical stage, early clinical stage and experimental drugs which are being developed for the treatment of Fabry disease by Amicus Therapeutics, Inc. and other companies. In addition, in May 2016, Galafold™ (migalastat), an oral small molecule pharmacological chaperone marketed by Amicus was approved in the European Union and other countries, but not in the United States, as a first line therapy for long-term treatment of adults and adolescents aged 16 years and older with a confirmed diagnosis of Fabry disease and who have an amenable mutation.

With respect to alidornase alfa, we face competition from Genentech Inc., a member of the Roche Group, which markets Pulmozyme.

With respect to PRX-106, we face competition from AbbVie Inc. (Humira), Johnson & Johnson and Merck & Co. (Remicade) and Pfizer and Amgen Inc. (Enbrel). In addition, we are aware of other clinical stage, early clinical stage and experimental antiTNF drugs.

We also face competition from companies that are developing other platforms for the expression of recombinant therapeutic pharmaceuticals. We are aware of companies that are developing alternative technologies to develop and produce therapeutic proteins in anticipation of the expiration of certain patent claims covering marketed proteins. Competitors developing alternative expression technologies include Crucell N.V. (which was acquired by Johnson & Johnson during 2010), Shire and GlycoFi, Inc. (which was acquired by Merck & Co. Inc.). Other companies are developing alternate plant-based technologies, include, among others, iBio, Inc., Medicago Inc., and Greenovation Biotech GmbH, none of which are cell-based. Rather, such companies base their product development on transgenic plants or whole plants. See “Risk Factors—Developments by competitors may render our products or technologies obsolete or non-competitive which would have a material adverse effect on our business, results of operations and financial condition.”

Scientific Advisory Board

We have reorganized our scientific advisory board by establishing a core team of advisors. The scientific advisory board may invite additional experts to attend meetings on a case-by-case basis. Members of our scientific advisory board consult with our management within their professional areas of expertise; exchange strategic and business development ideas with our management; attend scientific, medical and business meetings with our management, such as meetings with the FDA and comparable foreign regulatory authorities, meetings with strategic or potential strategic partners and other meetings relevant to their areas of expertise; and attend meetings of our scientific advisory board. We expect our scientific advisory board to convene at least twice annually, and we frequently consult with the individual members of our scientific advisory board. Our scientific advisory board currently includes the following people:

Name	**Affiliations (selected)**
Roger D. Kornberg, Ph.D. (Chairman)	Laureate of the Nobel Prize in Chemistry
	Member, U.S. National Academy of Sciences
	Winzer Professor of Medicine, Department of Structural Biology at Stanford University
	2001 Welch Prize (highest award granted in the field of chemistry in the United States)
	2002 Leopold Mayer Prize (the highest award granted in the field of biomedical sciences from the French Academy of Sciences)

Professor Aaron Ciechanover, M.D., D.Sc.	Laureate of the Nobel Prize in Chemistry
	Distinguished research Professor at the Cancer and Vascular Biology Research Center of the Rappaport Research Institute and Faculty of Medicine at the Technion, Israel's Institute of Technology
	American Academy of Arts and Sciences, Member
Alexander Levitzki, Ph.D.	Wolfson Family Professor of Biochemistry in the Department of Biological Chemistry of The Alexander Silberman Institute of Life Sciences, Hebrew University of Jerusalem
	American Association for Cancer Research, 2013 Award for Outstanding Achievement in Chemistry in Cancer Research.
	1990 Israel Prize in Biochemistry
	1990 Rothschild Prize in Biology

	2002 Hamilton-Fairley Award, European Society of Medical Oncology
	2005 Wolf Prize for Medicine
	2012 Nauta Award in Pharmacochemistry, The European Federation of Medicinal Chemistry (EFMC) (the highest award from the European Federation for Medicinal Chemistry)
Charles J. Arntzen, Ph.D.	Regent's Profession and Florence Ely Nelson Presidential Chair
	Biodesign Institute, CIDV, Arizona State University
	Member, National Academy of Sciences, USA
	American Society of Plant Biology Leadership in Science Public Service Award (2004)
	Botanical Society of America Centennial Award (2006)
	Fellow of American Society of Plant Biologists (2007)
	Doctor of Science *honoris causa.*, Hebrew University of Jerusalem
	Chair, Section O "Agriculture, Food, and Renewable Resources," American Association for the Advancement of Science (AAAS) (2011-2012)

Government Regulation

The testing, manufacture, distribution, advertising and marketing of drug products are subject to extensive regulation by federal, state and local governmental authorities in the United States, including the FDA, and by similar authorities in other countries. Any product that we develop must receive all relevant regulatory approvals or clearances, as the case may be, before it may be marketed in a particular country.

The regulatory process, which includes overseeing preclinical studies and clinical trials of each pharmaceutical compound to establish its safety and efficacy and confirmation by the FDA that good laboratory, clinical and manufacturing practices were maintained during testing and manufacturing, can take many years, requires the expenditure of substantial resources and gives larger companies with greater financial resources a competitive advantage over us. Delays or terminations of clinical trials that we undertake would likely impair our development of product candidates. Delays or terminations could result from a number of factors, including stringent enrollment criteria, slow rate of enrollment, size of patient population, having to compete with other clinical trials for eligible patients, geographical considerations and others.

The FDA review process can be lengthy and unpredictable, and we may encounter delays or rejections of our applications when submitted. Generally, in order to gain FDA approval, we must first conduct preclinical studies in a laboratory and in animal models to obtain preliminary information on a compound and to identify any potential safety problems. The results of these studies are submitted as part of an IND application that the FDA must review before human clinical trials of an investigational drug can commence. Clinical trials may be terminated by the clinical trial site, sponsor or the FDA if toxicities appear that are either worse than expected or unexpected.

Clinical trials are normally performed in three sequential phases and generally take two to five years, or longer, to complete. Phase I consists of testing the drug product in a small number of humans, normally healthy volunteers, to determine preliminary safety and tolerable dose range. Phase II usually involves studies in a limited patient population to evaluate the effectiveness of the drug product in humans having the disease or medical condition for which the product is indicated, determine dosage tolerance and optimal dosage and identify possible common adverse effects and safety risks. Phase III consists of additional controlled testing at multiple clinical sites to establish clinical safety and effectiveness in an expanded patient population of geographically dispersed test sites to evaluate the overall benefit-risk relationship for administering the product and to provide an adequate basis for product labeling. Phase IV clinical trials may be conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication.

After completion of clinical trials of a new drug product, FDA and foreign regulatory authority marketing approval must be obtained. Assuming that the clinical data support the product's safety and effectiveness for its intended use, a new drug application, or NDA, or a BLA is submitted to the FDA for review. Generally, it takes one to three years to obtain approval. If questions arise during the FDA review process, approval may take a significantly longer period of time. The testing and approval processes require substantial time and effort and approval on a timely basis, if at all, or the approval that we receive may be for a narrower indication than we had originally sought, potentially undermining the commercial viability of the product. Even if regulatory approvals are obtained, approved products are subject to continual review and holders of an approved product are required, for example, to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain requirements concerning advertising and promotional labeling for the product. Also, quality control and manufacturing procedures relating to a product must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to comply with cGMP and other aspects of regulatory compliance. The later discovery of previously unknown problems or failure to comply with the applicable regulatory requirements with respect to any product may result in restrictions on the marketing of the product or withdrawal of the product from the market as well as possible civil or criminal sanctions. See also "—International Regulation."

Under the Orphan Drug Act of 1983, the FDA may grant orphan drug designation to drugs and biological products intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. The FDA grants orphan drug designation to drugs that may provide a significant therapeutic advantage over existing treatments and target conditions affecting 200,000 or fewer U.S. patients per year. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. Among the other benefits of orphan drug designation are possible funding and tax savings to support clinical trials and for other financial incentives and a waiver of the marketing application user fee and most likely priority review. If a significant therapeutic advantage over existing treatments is shown in the marketing application, the FDA may grant orphan drug approval and provide a seven-year period of marketing exclusivity.

The FDA has a fast track program that is is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need, the purpose being to make important new drugs available to patients earlier. A drug candidate that receives Fast Track designation from the FDA is eligible for some or all of the following: more frequent meetings with the FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval; more frequent written communication from the FDA about such things as the design of the proposed clinical trials; eligibility for the FDA's Accelerated Approval and Priority Review, if relevant criteria are met; and eligibility for Rolling Review, which allows a drug company to submit completed sections of its BLA or NDA for review by the FDA, rather than waiting until every section of the BLA or NDA is completed before the entire application can be reviewed. BLA or NDA review usually does not begin until the drug company has submitted the entire application to the FDA. We used the Rolling Review option for our taliglucerase alfa NDA, which we completed in April 2010.

The United States federal government regulates healthcare through various agencies, including but not limited to the following: (i) the FDA, which administers the Federal Food, Drug, and Cosmetic Act (FDCA), as well as other

relevant laws; (ii) the Center for Medicare & Medicaid Services (CMS), which administers the Medicare and Medicaid programs; (iii) the Office of Inspector General (OIG) which enforces various laws aimed at curtailing fraudulent or abusive practices, including by way of example, the Anti-Kickback Law, the Anti-Physician Referral Law, commonly referred to as Stark, the Anti-Inducement Law, the Civil Money Penalty Law and the laws that authorize the OIG to exclude healthcare providers and others from participating in federal healthcare programs; and (iv) the Office of Civil Rights, which administers the privacy aspects of the Health Insurance Portability and Accountability Act of 1996, or HIPAA. All of the aforementioned are agencies within the Department of Health and Human Services (HHS). Healthcare is also provided or regulated, as the case may be, by the Department of Defense through its TriCare program, the Department of Veterans Affairs, especially through the Veterans Health Care Act of 1992, the Public Health Service within HHS under Public Health Service Act § 340B (42 U.S.C. § 256b), the Department of Justice through the Federal False Claims Act and various criminal statutes, and state governments under the Medicaid and other state sponsored or funded programs and their internal laws regulating all healthcare activities. Many states also have anti-kickback and anti-physician referral laws that are similar to the federal laws, but may be applicable in situations where federal laws do not apply.

Medicare is the federal healthcare program for those who are (i) over 65 years of age, (ii) disabled, (iii) suffering from end-stage renal disease or (iv) suffering from Lou Gehrig's disease. Medicare consists of part A, which covers inpatient costs, part B, which covers services by physicians and laboratories, durable medical equipment and certain drugs, primarily those administered by physicians, and part D, which provides drug coverage for most prescription drugs other than those covered under part B. Medicare also offers a managed care option under part C. Medicare is administered by CMS. In contrast, Medicaid is a state-federal healthcare program for the poor and is administered by the states pursuant to an agreement with the Secretary of Health and Human Services. Most state Medicaid programs cover most outpatient prescription drugs.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, PPACA, became law in the United States. PPACA substantially changes the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Key provisions of PPACA specific to the pharmaceutical industry, among others, include the following:

- An annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents into the United States, apportioned among these entities according to their market share in certain federal government healthcare programs (excluding sales of any drug or biologic product marketed for an orphan indication), beginning in 2011;

- An increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;

- A new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D, beginning in 2011;

- Extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, effective March 23, 2010;

- Expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in April 2010 and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;

- Expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective January 2010;

- New requirements to report certain financial arrangements with physicians and others, including reporting any "transfer of value" made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2012, with reporting starting in 2013;

- A new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;

- A licensure framework for follow-on biologic products; and

- A new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

International Regulation

We are subject to regulations and product registration requirements in many foreign countries in which we may sell our products, including in the areas of product standards, packaging requirements, labeling requirements, import and export restrictions and tariff regulations, duties and tax requirements. The time required to obtain clearance required by foreign countries may be longer or shorter than that required for FDA clearance, and requirements for licensing a product in a foreign country may differ significantly from FDA requirements.

Pharmaceutical products may not be imported into, or manufactured or marketed in, the State of Israel absent drug registration. The three basic criteria for the registration of pharmaceuticals in Israel is quality, safety and efficacy of the pharmaceutical product and the Israeli MOH requires pharmaceutical companies to conform to international developments and standards. Regulatory requirements are constantly changing in accordance with scientific advances as well as social and ethical values.

The relevant legislation of the European Union requires that medicinal products, including generic versions of previously approved products, and new strengths, dosage forms and formulations, of previously approved products, shall have a marketing authorization before they are placed on the market in the European Union. Authorizations are granted after the assessment of quality, safety and efficacy by the respective health authorities. In order to obtain an authorization, an application must be made to the competent authority of the member state concerned or in a centralized procedure to the EMA. Besides various formal requirements, the application must contain the results of pharmaceutical (physico-chemical, biological or microbiological) tests, of preclinical (toxicological and pharmacological) tests as well as of clinical trials. All of these tests must have been conducted in accordance with relevant EU regulations and must allow the reviewer to evaluate the quality, safety and efficacy of the medicinal product. Orphan drug designation in the European Union is granted to medicinal products intended for the diagnosis, prevention and treatment of life-threatening diseases and very serious conditions that affect not more than five in 10,000 people in the European Union. Orphan drug designation is generally given to medicinal products that treat conditions for which no current therapy exists or are expected to bring a significant benefit to patients over existing therapies.

Israeli Government Programs

The following is a summary of the current principal Israeli tax laws applicable to us and Protalix Ltd., and of the Israeli Government programs from which Protalix Ltd. benefits. Some parts of this discussion are based on new tax legislation that has not been subject to judicial or administrative interpretation. Therefore, the views expressed in the discussion may not be accepted by the tax authorities in question. The discussion should not be construed as legal or professional tax advice and does not cover all possible tax considerations.

General Corporate Tax Structure in Israel

The income of Protalix Ltd., other than income from "Approved Enterprises," is taxed in Israel at the regular rates which were 26.5% for fiscal year 2015, 25% in 2016 and 24% in 2017.

In January 2016, the Law for the Amendment of the Income Tax Ordinance (No. 216) was published, enacting a reduction of corporate tax rate beginning in 2016 and thereafter, from 26.5% to 25%. In December 2016, the Economic Efficiency Law (Legislative Amendments for Implementing the Economic Policy for the 2017 and 2018 Budget Year), 2016 was published, introducing a gradual reduction in corporate tax rate from 25% to 23%. However, the law also included a temporary provision setting the corporate tax rate in 2017 at 24%. As a result, the corporate tax rate was 24% in 2017 and will be 23% in 2018 and thereafter.

Capital gains on the sale of assets are subject to capital gains tax according to the corporate tax rate in effect in the year which the assets are sold.

Law for the Encouragement of Capital Investments, 1959

The Law for the Encouragement of Capital Investments, 1959, as amended, or the Investment Law, provides certain incentives for capital investments in a production facility (or other eligible assets). Generally, an investment program that is implemented in accordance with the provisions of the Investment Law, referred to as an "Approved Enterprise," is entitled to benefits. These benefits may include cash grants from the Israeli government and tax benefits, based upon, among other things, the location of the facility in which the investment is made and specific elections made by the grantee.

Protalix Ltd. will continue to enjoy the tax benefits under the pre-revision provisions of the Investment Law. If any new benefits are granted to Protalix Ltd. in the future, Protalix Ltd. will be subject to the provisions of the amended Investment Law with respect to these new benefits. Therefore, the following discussion is a summary of the Investment Law prior to its amendment as well as the relevant changes contained in the new legislation.

Under the Investment Law prior to its amendment, a company that wished to receive benefits had to receive approval from the Authority for the Investment and Development of the Industry and Economy, or the Authority. Each certificate of approval for an Approved Enterprise relates to a specific investment program in the Approved Enterprise, delineated both by the financial scope of the investment and by the physical characteristics of the facility or the asset, e.g., the equipment to be purchased and utilized pursuant to the program.

An Approved Enterprise may elect to forego any entitlement to the grants otherwise available under the Investment Law and, instead, participate in an alternative benefits program under which the undistributed income from the Approved Enterprise is fully exempt from corporate tax for a defined period of time. Under the alternative package of benefits, a company's undistributed income derived from an Approved Enterprise will be exempt from corporate tax for a period of between two and 10 years from the first year of taxable income, depending upon the geographic location within Israel of the Approved Enterprise. Upon expiration of the exemption period, the Approved Enterprise is eligible for the reduced tax rates otherwise applicable under the Investment Law for any remainder of the otherwise applicable benefits period (up to an aggregate benefits period of either seven or 10 years, depending on the location of the company or its definition as a foreign investors' company). If a company has more than one Approved Enterprise program or if only a portion of its capital investments are approved, its effective tax rate is the result of a weighted combination of the applicable rates. The tax benefits from any certificate of approval relate only to taxable profits attributable to the specific Approved Enterprise. Income from activity that is derived from different Approved Enterprises does not enjoy these tax benefits.

A company that has an Approved Enterprise program is eligible for further tax benefits if it qualifies as a foreign investors' company. A foreign investors' company eligible for benefits is essentially a company in which more than 25% of the share capital (in terms of shares, rights to profit, voting and appointment of directors) is owned (measured by both share capital and combined share and loan capital) by non-Israeli residents. A company that qualifies as a foreign investors' company and has an Approved Enterprise program is eligible for tax benefits for a 10-year benefit period and may enjoy a reduced corporate tax rate of 10% to 25%, depending on the amount of the company's shares held by non-Israeli shareholders.

If a company that has an Approved Enterprise program is a wholly owned subsidiary of another company, the percentage of foreign investments is determined based on the percentage of foreign investment in the parent company. The tax rates and related levels of foreign investments are set forth in the following table:

Percent of Foreign Ownership	Rate of Reduced Tax
0-49%	25%
49-74%	20%
74-90%	15%
90-100%	10%

Our original facility in Israel has been granted “Approved Enterprise” status, and it has elected to participate in the alternative benefits program. Under the terms of its Approved Enterprise program, the facility is located in a top priority location, or “Zone A,” and, therefore, the income from that Approved Enterprise will be tax exempt in Israel for a period of 10 years, commencing with the year in which taxable income is first generated from the relevant Approved Enterprise. The current benefits program may not continue to be available and Protalix Ltd. may not continue to qualify for its benefits.

A company that has elected to participate in the alternative benefits program and that subsequently pays a dividend out of the income derived from the Approved Enterprise during the tax exemption period will be subject to corporate tax in respect of the amount distributed at the rate that would have been applicable had the company not elected the alternative benefits program (generally 10% to 25%, depending on the extent to which non-Israeli shareholders hold such company's shares). If the dividend is distributed within 12 years after the commencement of the benefits period (or, in the case of a foreign investor's company, without time limitation), the dividend recipient is taxed at the reduced withholding tax rate of 15% applicable to dividends from approved enterprises, or at the lower rate under an applicable tax treaty. After this period, the withholding tax rate is 25%, or at the lower rate under an applicable tax treaty. In the case of a company with a foreign investment level (as defined by the Investment Law) of 25% or more, the 12-year limitation on reduced withholding tax on dividends does not apply. The company must withhold this tax at its source, regardless of whether the dividend is converted into foreign currency.

The Investment Law also provides that an Approved Enterprise is entitled to accelerated depreciation on its property and equipment that are included in an approved investment program. This benefit is an incentive granted by the Israeli government regardless of whether the alternative benefits program is elected.

The benefits available to an Approved Enterprise are conditioned upon terms stipulated in the Investment Law and regulations and the criteria set forth in the applicable certificate of approval. If Protalix Ltd. does not fulfill these conditions in whole or in part, the benefits can be canceled and Protalix Ltd. may be required to refund the received benefits, linked to the Israeli consumer price index with the addition of interest or alternatively with an additional penalty payment. We believe that Protalix Ltd. currently operates in compliance with all applicable conditions and criteria, but there can be no assurance that Protalix Ltd. will continue to do so. Furthermore, there can be no assurance that any Approved Enterprise status granted to Protalix Ltd.'s facilities will entitle Protalix Ltd. to the same benefits to which it is currently entitled.

Under the Investment Law, the approval of the Authority is required only for Approved Enterprises that receive cash grants. Approved Enterprises that do not receive benefits in the form of governmental cash grants, but only tax benefits, are no longer required to obtain this approval. Instead, these Approved Enterprises are required to make certain investments as specified in the Investment Law.

The amended Investment Law specifies certain conditions for an Approved Enterprise to be entitled to benefits. These conditions include:

- the Approved Enterprise's revenues from any single country or a separate customs territory may not exceed 75% of the Approved Enterprise's total revenues; or

- at least 25% of the Approved Enterprise's revenues during the benefits period must be derived from sales into a single country or a separate customs territory with a population of at least 14 million.

There can be no assurance that Protalix Ltd. will comply with the above conditions in the future or that Protalix Ltd. will be entitled to any additional benefits under the Investment Law. In addition, it is possible that Protalix Ltd. may not be able to operate in a manner that maximizes utilization of the potential benefits available under the Investment Law.

From time to time, the Israeli Government has considered reducing the benefits available to companies under the Investment Law. The termination or substantial reduction of any of the benefits available under the Investment Law could materially impact the cost of our future investments.

Encouragement of Industrial Research, Development and Technology Innovation Law, 1984

To date, Protalix Ltd. has received grants from the OCS under the Israeli Law for the Encouragement of Industrial Research, Development and Technology Innovation, 1984, and related regulations, or the Research Law. On January 1, 2016, the Israeli government established NATI which replaced many of the functions of the Office of the Chief Scientist of the Israeli Department of Labor, or the OCS. For purposes of clarity, references to NATI will include the OCS. NATI grants are made available to finance of a portion of Protalix Ltd.'s research and development expenditures in Israel. As of December 31, 2017, NATI approved grants in respect of Protalix Ltd.'s continuing operations totaling approximately $50.9 million, measured from inception. Protalix Ltd. is required to repay up to 100% of grants actually received (plus interest at the LIBOR rate applied to the grants received on or after January 1, 1999) to NATI through payments of royalties at a rate of 3% to 6% of the revenues generated from NATI-funded project, depending on the period in which revenues were generated. As of December 31, 2017, Protalix Ltd. either paid or accrued royalties payable of $8.7 million and Protalix Ltd.'s contingent liability to NATI with respect to grants received was approximately $42.2 million.

Under the Research Law, recipients of grants from NATI are prohibited from manufacturing products developed using these grants outside of the State of Israel without special approvals, although the Research Law does enable companies to seek prior approval for conducting manufacturing activities outside of Israel without being subject to increased royalties. If Protalix Ltd. receives approval to manufacture the products developed with government grants outside of Israel, it will be required to pay an increased total amount of royalties (possibly up to 300% of the grant amounts plus interest), depending on the manufacturing volume that is performed outside of Israel, as well as at a possibly increased royalty rate.

Additionally, under the Research Law, Protalix Ltd. is prohibited from transferring NATI-financed technologies and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the approval of NATI Council or the Research Committee. Protalix Ltd. may not receive the required approvals for any proposed transfer and, if received, Protalix Ltd. may be required to pay NATI a portion of the consideration that it receives upon any sale of such technology by a non-Israeli entity. The scope of the support received, the royalties that Protalix Ltd. has already paid to NATI, the amount of time that has elapsed between the date on which the know-how was transferred and the date on which NATI grants were received and the sale price and the form of transaction will be taken into account in order to calculate the amount of the payment to NATI. Approval of the transfer of technology to residents of the State of Israel is required, and may be granted in specific circumstances only if the recipient abides by the provisions of applicable laws, including the restrictions on the transfer of know-how and the obligation to pay royalties. No assurance can be made that approval to any such transfer, if requested, will be granted.

Under the Research Law and the regulations promulgated thereunder, NATI Council may allow the transfer outside of Israel of know-how derived from an approved program and the related manufacturing rights in limited circumstances which are currently as follows:

- in the event of a sale of know-how itself to a non-affiliated third party, provided that upon such sale the owner of the know-how pays to NATI an amount, in cash, as set forth in the Research Law (and the regulations promulgated thereunder). In addition, the amendment provides that if the purchaser of the know-how gives the selling Israeli company the right to exploit the know-how by way of an exclusive, irrevocable and unlimited license, the research committee may approve such transfer in special cases without requiring a cash payment.

- in the event of a sale of a company which is the owner of know-how, pursuant to which the company ceases to be an Israeli company, provided that upon such sale, the owner of the know-how makes a cash payment to NATI as set forth in the Research Law (and the regulations promulgated thereunder).

- in the event of an exchange of know-how such that in exchange for the transfer of know-how outside of Israel, the recipient of the know-how transfers other know-how to the company in Israel in a manner in which NATI is convinced that the Israeli economy realizes a greater, overall benefit from the exchange of know-how.

The Research Committee may, in special cases, approve the transfer of manufacture or of manufacturing rights of a product developed within the framework of the approved program or which results therefrom, outside of Israel.

The State of Israel does not own intellectual property rights in technology developed with NATI funding and there is no restriction on the export of products manufactured using technology developed with NATI funding. The technology is, however, subject to transfer of technology and manufacturing rights restrictions as described above. For a description of such restrictions, please see "Risk Factors—Risks Relating to Our Operations in Israel." NATI approval is not required for the export of any products resulting from the research or development or for the licensing of any technology in the ordinary course of business.

Law for the Encouragement of Industry (Taxes), 1969

We believe that Protalix Ltd. currently qualifies as an "Industrial Company" within the meaning of the Law for the Encouragement of Industry (Taxes), 1969, or the Industry Encouragement Law. The Industry Encouragement Law defines "Industrial Company" as a company resident in Israel and incorporated in Israel, that derives 90% or more of its income in any tax year (other than specified kinds of passive income such as capital gains, interest and dividends) from an "Industrial Enterprise" operating in Israel (including Judea & Samaria territories and the Gaza strip), that it owns. An "Industrial Enterprise" is defined as an enterprise whose major activity in a given tax year is industrial production.

The following corporate tax benefits, among others, are available to Industrial Companies:

- amortization of the cost of purchased know-how and patents over an eight-year period for tax purposes;
- accelerated depreciation rates on equipment and buildings;
- under specified conditions, an election to file consolidated tax returns with other related Israeli Industrial Companies; and
- expenses related to a public offering are deductible in equal amounts over three years.

Eligibility for the benefits under the Industry Encouragement Law is not subject to receipt of prior approval from any governmental authority. It is possible that Protalix Ltd. may fail to qualify or may not continue to qualify as an "Industrial Company" or that the benefits described above will not be available in the future.

Tax Benefits for Research and Development

Under specified conditions, Israeli tax laws allow a tax deduction by a company for research and development expenditures, including capital expenditures, for the year in which such expenditures are incurred. These expenditures must relate to scientific research and development projects and must be approved by NATI. Furthermore, the research and development projects must be for the promotion of the company and carried out by or on behalf of the company seeking such tax deduction. However, the amount of such deductible expenditures is reduced by the sum of any funds received through government grants for the finance of such scientific research and development projects. Expenditures not so approved are deductible over a three-year period.

Employees

As of December 31, 2017, we had 190 employees, of whom 21 have a Ph.D. or an M.D.in their respective scientific fields. We believe that our relations with these employees are good. We believe that our success will greatly depend on our ability to identify, attract and retain capable employees. The Israeli Ministry of Labor and Welfare is authorized to make certain industry-wide collective bargaining agreements, or Expansion Orders, that apply to types of industries or employees including ours. These agreements affect matters such as cost of living adjustments to salaries, length of working hours and week, recuperation, travel expenses, and pension rights. Otherwise, our

employees are not represented by a labor union or represented under a collective bargaining agreement. See “Risk Factors—We depend upon key employees and consultants in a competitive market for skilled personnel. If we are unable to attract and retain key personnel, it could adversely affect our ability to develop and market our products.”

Company Background

Our principal business address is set forth below. Our executive offices and our main research manufacturing facility are located at that address. Our telephone number is +972-4-988-9488. We were originally incorporated in the State of Florida in April 1992, and reincorporated in the State of Delaware in March 2016. Protalix Ltd., our wholly-owned subsidiary and sole operating unit, is an Israeli company and was originally incorporated in Israel on December 27, 1993. During 1999, Protalix Ltd. changed its focus from plant secondary metabolites to the expression of recombinant therapeutic proteins in plant cells, and in April 2004 changed its name to Protalix Ltd.

ProCellEx® is our registered trademark. Each of the other trademarks, trade names or service marks appearing in this Annual Report on Form 10-K belongs to its respective holder.

Available Information

Our corporate website is www.protalix.com. We make available on our website, free of charge, our Commission filings, including our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports, as soon as reasonably practicable after we electronically file these documents with, or furnish them to, the Commission. Additionally, from time to time, we provide notifications of material news including press releases and conferences on our website. Webcasts of presentations made by our company at certain conferences may also be available from time to time on our website, to the extent the webcasts are available. The content of our website is not intended to be incorporated by reference into this report or in any other report or document we file and any references to these websites are intended to be inactive textual references only.

We are also listed on the Tel Aviv Stock Exchange, or the TASE, and, accordingly, we submit copies of all our filings with the Commission to the Israeli Securities Authority and the TASE. Such copies can be retrieved electronically through the TASE's internet messaging system (www.maya.tase.co.il) and through the MAGNA distribution site of the Israeli Securities Authority (www.magna.isa.gov.il).

Our website also includes printable versions of our Code of Business Conduct and Ethics and the charters for each of the Audit, Compensation and Nominating Committees of our Board of Directors. Each of these documents is also available in print, free of charge, to any shareholder who requests a copy by addressing a request to:

Protalix BioTherapeutics, Inc.

2 Snunit Street, Science Park

P.O. Box 455

Carmiel 20100, Israel

Attn: Mr. Yossi Maimon, Chief Financial Officer

Item 1A. Risk Factors

You should carefully consider the risks described below together with the other information included in this Annual Report on Form 10-K. Our business, financial condition or results of operations could be adversely affected by any of these risks. If any of these risks occur, the value of our common stock could decline.

Risks Related to Clinical Trials and Regulatory Matters

Clinical trials are very expensive, time-consuming and difficult to design and implement and may result in unforeseen costs which may have a material adverse effect on our business, results of operations and financial condition.

Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time-consuming. Other than taliglucerase alfa, all of our other drug candidates, including pegunigalsidase alfa, are in the clinical, preclinical or research stages and will take at least several years to complete. Preliminary and initial results from a clinical trial do not necessarily predict final results, and failure can occur at any stage of the trial. We may encounter problems that cause us to abandon or repeat preclinical studies or clinical trials. Failure or delay in the commencement or completion of our clinical trials may be caused by several factors, including:

- slower than expected rates of patient recruitment, particularly with respect to trials of rare diseases such as Fabry disease;
- determination of dosing issues;
- unforeseen safety issues;
- lack of effectiveness during clinical trials;
- disagreement by applicable regulatory bodies over our trial protocols, our the interpretation of data from preclinical studies or clinical trials or conduct and control of clinical trials;
- determination that the patient population participating in a clinical trial may not be sufficiently broad or representative to assess efficacy and safety for our target population;
- inability to monitor patients adequately during or after treatment;
- inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; and
- lack of sufficient funding to finance the clinical trials.

Any failure or delay in commencement or completion of any clinical trials of pegunigalsidase alfa or our other product candidates will have a material adverse effect on our business, results of operations and financial condition. In addition, we or the FDA or other regulatory authorities may suspend any clinical trial at any time if it appears that we

are exposing participants in the trial to unacceptable safety or health risks or if the FDA or such other regulatory authorities, as applicable, find deficiencies in our IND submissions or the conduct of the trial. Any suspension of a clinical trial may have a material adverse effect on our business, results of operations and financial condition.

We may find it difficult to enroll patients in our clinical trials, which could cause significant delays in the completion of such trials or may cause us to abandon one or more clinical trials.

Some of the diseases or disorders that our drug candidates are intended to treat, such as Fabry disease, are relatively rare and we expect only a subset of the patients with these diseases to be eligible for our clinical trials. Our clinical trials generally mandate that a patient cannot be involved in another clinical trial for the same indication. Therefore, subjects that participate in ongoing clinical trials for products that are competitive with our drug candidates are not available for our clinical trials. An inability to enroll a sufficient number of patients for our ongoing phase III clinical trials of pegunigalsidase alfa, or for any of our other current or future clinical trials, would result in significant delays or may require us to abandon one or more clinical trials altogether, which will have a material adverse effect on our business, results of operations and financial condition.

If the results of our clinical trials do not support our claims relating to a drug candidate, or if serious side effects are identified, the completion of development of such drug candidate may be significantly delayed or we may be forced to abandon development altogether, which will significantly impair our ability to generate product revenues.

The results of our clinical trials with respect to any drug candidate might not support our claims of superiority, safety or efficacy, the effects of our drug candidates may not be the desired effects or may include undesirable side effects or the drug candidates may have other unexpected characteristics. Further, success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and the results of later clinical trials may not replicate the results of prior clinical trials and preclinical testing. Data obtained from tests are susceptible to varying interpretations which may delay, limit or prevent regulatory approval. The clinical trial process may fail to demonstrate that our drug candidates are safe for humans and effective for indicated uses. In addition, our clinical trials, particularly with respect to pegunigalsidase alfa, may involve specific and small patient populations. Results of early clinical trials conducted on a small patient population may not be indicative of future results. Adverse or inconclusive results may cause us to abandon a drug candidate and may delay development of other drug candidates. Any delay in, or termination of, our clinical trials will delay the filing of NDAs and BLAs with the FDA, or other filings with other foreign regulatory authorities, and, ultimately, significantly impair our ability to commercialize our drug candidates and generate product revenues which would have a material adverse effect on our business, results of operations and financial condition.

Patients may discontinue their participation in our clinical trials which may negatively impact the results of these studies and extend the timeline for completion of our development programs.

Patients enrolled in our clinical trials may discontinue their participation at any time during the study as a result of a number of factors, including withdrawing their consent, experiencing adverse clinical events, which may or may not be judged related to our drug candidates under evaluation, or due to planned or actual pregnancies. The discontinuation of patients in any one of our studies may delay the completion of the study or cause the results from the study not to be positive or to not support a filing for regulatory approval of the applicable drug candidate, which would have a material adverse effect on our business, results of operations and financial condition.

Because our clinical trials depend upon third-party researchers, the results of our clinical trials and such research activities are subject to delays and other risks which are, to a certain extent, beyond our control, which could impair our clinical development programs and our competitive position.

We depend upon independent investigators and collaborators, such as universities and medical institutions, to conduct our preclinical and clinical trials. These collaborators are not our employees, and we cannot control the amount or timing of resources that they devote to our clinical development programs. The investigators may not assign as great a

priority to our clinical development programs or pursue them as diligently as we would if we were undertaking such programs directly. If outside collaborators fail to devote sufficient time and resources to our clinical development programs, or if their performance is substandard, the approval of anticipated NDAs, BLAs and other marketing applications, and our introduction of new drugs, if any, may be delayed which could impair our clinical development programs and would have a material adverse effect on our business and results of operations. The collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators also assist our competitors, our competitive position could be harmed.

We are subject to extensive governmental regulation including the requirements of the FDA and other comparable regulatory authorities before our drug candidates may be marketed.

Both before and after marketing approval of our drug candidates, if at all, we, our drug candidates, our suppliers, our contract manufacturers and our contract testing laboratories are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. Failure to comply with applicable requirements of the FDA or comparable foreign regulatory authorities could result in, among other things, any of the following actions:

- warning letters;
- fines and other monetary penalties;
- unanticipated expenditures;
- delays in the FDA's or other foreign regulatory authorities' approving, or the refusal of any regulatory authority to approve, any drug candidate;

- product recall or seizure;
- interruption of manufacturing or clinical trials;
- operating restrictions;
- injunctions; and
- criminal prosecutions.

In addition to the approval requirements, other numerous and pervasive regulatory requirements apply, both before and after approval, to us, our drug candidates, and our suppliers, contract manufacturers, and contract laboratories. These include requirements related to:

- testing;
- manufacturing;
- quality control;
- labeling;
- advertising;
- promotion;
- distribution;
- export;
- reporting to the FDA certain adverse experiences associated with use of the drug candidate; and
- obtaining additional approvals for certain modifications to the drug candidate or its labeling or claims.

We also are subject to inspection by the FDA and comparable foreign regulatory authorities, to determine our compliance with regulatory requirements, as are our suppliers, contract manufacturers, and contract testing laboratories, and there can be no assurance that the FDA or any other comparable foreign regulatory authority, will not identify compliance issues that may disrupt production or distribution, or require substantial resources to correct. We may be required to make modifications to our manufacturing operations in response to these inspections which may require significant resources and may have a material adverse effect upon our business, results of operations and financial condition.

The approval process for any drug candidate may also be delayed by changes in government regulation, future legislation or administrative action or changes in policy of the FDA and comparable foreign authorities that occur prior to or during their respective regulatory reviews of such drug candidate. Delays in obtaining regulatory approvals with respect to any drug candidate may:

- delay commercialization of, and our ability to derive product revenues from, such drug candidate;
- delay any regulatory-related milestone payments payable under outstanding collaboration agreements;
- require us to perform costly procedures with respect to such drug candidate; or
- otherwise diminish any competitive advantages that we may have with respect to such drug candidate.

Delays in the approval process for any drug candidate may have a material adverse effect upon our business, results of operations and financial condition.

We may not obtain the necessary U.S., EMA or other worldwide regulatory approvals to commercialize our drug candidates in a timely manner, if at all, which would have a material adverse effect on our business, results of operations and financial condition.

We need FDA approval to commercialize our drug candidates in the United States, EMA approval to commercialize our drug candidates in the European Union and approvals from other foreign regulators to commercialize our drug candidates elsewhere. In order to obtain FDA approval of any of our drug candidates, we must submit to the FDA an NDA or a BLA demonstrating that the drug candidate is safe for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials. In the European Union, we must submit an MAA to the EMA. Satisfaction of the regulatory requirements of the FDA, EMA and other foreign regulatory authorities typically takes many years, depends upon the type, complexity and novelty of the drug candidate and requires substantial resources for research, development and testing. Even if we comply with all the requests of regulatory authorities, the authorities may ultimately reject any marketing application that we file for a product candidate in the future, if any, or we might not obtain regulatory clearance in a timely manner. Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced or late-stage clinical trials, even after obtaining promising earlier trial results or in preliminary findings or other comparable authorities for such clinical trials. Further, even if favorable testing data is generated by the clinical trials of a drug candidate, the applicable regulatory authority may not accept or approve the marketing application filed by a pharmaceutical or biotechnology company for the drug candidate. Failure to obtain approval of the FDA, EMA or comparable foreign authorities of any of our drug candidates in a timely manner, if at all, will severely undermine our business, financial condition and results of operation by reducing our potential marketable products and our ability to generate corresponding product revenues.

Our research and clinical efforts may not result in drugs that the FDA, EMA or foreign regulatory authorities consider safe for humans and effective for indicated uses, which would have a material adverse effect on our business, results of operations and financial condition. After clinical trials are completed for any drug candidate, if at all, the FDA, EMA and foreign regulatory authorities have substantial discretion in the drug approval process of the drug candidate in their respective jurisdictions and may require us to conduct additional clinical testing or perform post-marketing studies which would cause us to incur additional costs. Incurring such costs may have a material adverse effect on our business, results of operations and financial condition.

We have only limited experience in regulatory affairs, and some of our drug candidates may be based on new technologies. These factors may affect our ability or the time we require to obtain necessary regulatory approvals.

We have only limited experience in filing and prosecuting the applications necessary to gain regulatory approvals for medical devices and drug candidates. Moreover, some of the drug candidates that are likely to result from our development programs may be based on new technologies that have not been extensively tested in humans. The regulatory requirements governing these types of drug candidates may be less well defined or more rigorous than for

conventional products. As a result, we may experience a longer regulatory process in connection with obtaining regulatory approvals of any products that we develop.

Orphan drug designation may not ensure that we will enjoy market exclusivity in any jurisdiction. If any of our other competitors are able to obtain orphan drug exclusivity for any products that are competitive with our products, we may be precluded from selling or obtaining approval of our competing products by the applicable regulatory authorities for a significant period of time.

In the United States, the European Union and other countries, a drug may be designated as having orphan drug status, subject to certain conditions. There can be no assurance that a drug candidate that receives orphan drug designation will receive orphan drug marketing exclusivity and more than one drug can have orphan designation for the same indication. In addition, the orphan drug designation granted to pegunigalsidase alfa by the EMA does not affect Fabry disease treatments that preexist the approval of pegunigalsidase alfa, if at all.

Foreign regulations regarding orphan drugs are similar to those in the United States but there are several differences. For example, the exclusivity period in the European Union is generally 10 years. From time to time, we may apply to the FDA or any comparable foreign regulatory authority for orphan drug designation for any one or more of our drug candidates. Other than pegunigalsidase alfa which was granted orphan drug designation by the EMA, none of our drug candidates have been designated as an orphan drug and there is no guarantee that the FDA or any other regulatory authority will grant such designation in the future. In addition, neither orphan drug designation nor orphan drug exclusivity prevents competitors from developing or marketing different drugs for the relevant indication. Even if we obtain orphan drug exclusivity for one or more indications for one of our drug candidates, we may not be able to maintain the exclusivity. For example, if a competitive product that is the same drug or biologic as one of our drug candidates is shown to be clinically superior to the drug candidate, any orphan drug exclusivity granted to the drug candidate will not block the approval of the competitive product.

If any drug receives orphan drug exclusivity in any jurisdiction for the same indication of any of our drug candidates, we may be prevented from attaining a similar designation with respect to our drug candidate or from marketing the drug candidate in the jurisdiction during the applicable exclusivity period, which will have a material adverse effect on our business, results of operations and financial condition.

The fast track designation for pegunigalsidase alfa for the treatment of Fabry disease may not lead to a faster development or regulatory review or approval process or increase the likelihood that pegunigalsidase alfa will receive regulatory approval for the treatment of Fabry disease.

In January 2018, the FDA granted Fast Track designation to pegunigalsidase alfa for the treatment of Fabry disease. A drug that receives Fast Track designation from the FDA is eligible for certain benefits. However, fast track designation does not increase the likelihood that pegunigalsidase alfa will receive regulatory approval for the treatment of Fabry disease. Further, despite the designation, we may not experience a faster development process, review or approval compared to applications considered for approval under conventional FDA procedures. In addition, the FDA is entitled to withdraw the Fast Track designation of a drug candidate at any time. Any failure to realize the benefits of fast track designation may have a material adverse effect on our business, results of operations and financial condition.

Risks Related to Our Business

We have a limited operating history which may limit the ability of investors to make an informed investment decision.

Taliglucerase alfa is our only product with commercial approvals. The successful commercialization of our other drug candidates will require us to perform a variety of functions, including:

- continuing to perform preclinical development and clinical trials;
- participating in regulatory approval processes;
- formulating and manufacturing products; and
- conducting sales and marketing activities.

Our operations have been limited to organizing and staffing our company, acquiring, developing and securing our proprietary technology and undertaking, through third parties, preclinical trials and clinical trials of our principal drug candidates. To date, our phase III clinical trial of taliglucerase alfa is the only phase III study we have completed. These operations provide a limited basis for investors to assess our ability to commercialize our drug candidates and whether to invest in our company.

We currently depend heavily on the success of pegunigalsidase alfa. Any failure to commercialize pegunigalsidase alfa, or the experience of significant delays in doing so, will have a material adverse effect on our business, results of operations and financial condition.

We are investing a significant portion of our efforts and financial resources in the development of pegunigalsidase alfa and our ability to generate significant product revenues in the future, will depend heavily on the successful development and commercialization of pegunigalsidase alfa. The successful commercialization of pegunigalsidase alfa will depend on several factors, including the following:

- successful completion of our ongoing studies of pegunigalsidase alfa;
- Chiesi's efforts under the Chiesi Agreement;
- obtaining marketing approvals from the FDA, the EMA and other foreign regulatory authorities;
- maintaining the cGMP compliance of our manufacturing facility or establishing manufacturing arrangements with third parties;
- the successful audit of our facilities by the FDA and other foreign regulatory authorities;
- our development of a successful sales and marketing organization for pegunigalsidase in the United States;
- the availability of reimbursement to patients from healthcare payors for pegunigalsidase alfa, if approved;
- a continued acceptable safety and efficacy profile of pegunigalsidase alfa following approval; and
- other risks described in these Risk Factors.

Any failure to commercialize pegunigalsidase alfa or the experience of significant delays in doing so will have a material adverse effect on our business, results of operations and financial condition.

Any failure by us to supply drug substance to Pfizer may have a material adverse effect on our business, results of operations and financial condition.

Under the Amended Pfizer Agreement, we have agreed, for the first 10-year period after the execution of the agreement, to sell drug substance to Pfizer for the production of Elelyso, and Pfizer maintains the right to extend the supply period for up to two additional 30-month periods subject to certain terms and conditions. As part of that obligation, we agreed to substantial financial penalties in case we fail to comply with the supply commitments, or are delayed in doing so. The amounts of the penalties depend on when any such failure occurs and for how long it persists, if at all, and other considerations. Any failure to comply with the supply commitments under the Amended Pfizer Agreement may have a material adverse effect on our business, results of operations and financial condition.

Our strategy, in certain cases, is to enter into collaboration agreements with third parties to leverage our ProCellEx system to develop product candidates. If we fail to enter into these agreements or if we or the third parties do not perform under such agreements or terminate or elect to discontinue the collaboration, it could have a material adverse effect on our revenues.

Our strategy, in certain cases, is to enter into arrangements with pharmaceutical companies to leverage our ProCellEx system to develop additional product candidates. Under these arrangements, we may grant to our partners rights to license and commercialize pharmaceutical products developed under the applicable agreements, as we have done with pegunigalsidase alfa. Our partners may control key decisions relating to the development of the products and we may depend on our partners' expertise and dedication of sufficient resources to develop and commercialize our product candidates. The rights of our partners limit our flexibility in considering alternatives for the commercialization of our product candidates. If we or any of our current or future partners breach or terminate the agreements that make up such arrangements, our partners otherwise fail to conduct their obligations under such arrangements in a timely manner, there is a dispute about their obligations or if either party terminates the applicable agreement or elects not to continue the arrangement, we may not enjoy the benefits of the agreements or receive a sufficient amount of royalty or milestone payments from them, if any, which may have a material adverse effect on our business, results of operations and financial condition.

If we are unable to develop and commercialize our product candidates, our business will be adversely affected.

A key element of our strategy is to develop and commercialize a portfolio of new products in addition to taliglucerase alfa. We seek to do so through our internal research programs and strategic collaborations for the development of new products. Research programs to identify new product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- a product candidate is not capable of being produced in commercial quantities at an acceptable cost, or at all;
- a product candidate may not be accepted by patients, the medical community or third-party payors;
- competitors may develop alternatives that render our product candidates obsolete;
- the research methodology used may not be successful in identifying potential product candidates; or
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory approval.

Any failure to develop or commercialize any of our other product candidates may have a material adverse effect on our business, results of operations and financial condition.

Our ProCellEx protein expression system is based on our proprietary plant cell-based expression technology which has a limited history and any material problems with the system, which may be unforeseen, may have a material adverse effect on our business, results of operations and financial condition.

Our ProCellEx protein expression system is based on our proprietary plant cell-based expression technology. The success of our business is dependent upon the successful development and approval of our product and product candidates produced through this technology. Although taliglucerase alfa and all of our product candidates are produced through ProCellEx, the technology remains novel. Accordingly, the technology remains subject to certain risks. Mammalian cell-based protein expression systems have been used in connection with recombinant therapeutic protein expression for more than 30 years and are the subject of a wealth of data; in contrast, there is not a significant amount of data generated regarding plant cell-based protein expression and, accordingly, plant cell-based protein expression systems may be subject to unknown risks. In addition, the protein glycosilation pattern created by our protein expression system is not identical to the natural human glycosilation pattern and, although to date clinical data for up to five years, and commercial data for an additional five years, on taliglucerase alfa has not demonstrated any sign of any effect, the longer term effect of the protein glycosilation pattern created by our protein expression system on human patients, if any, is still unknown. Lastly, as our protein expression system is a new technology, we cannot always rely on existing equipment; rather, there is a need to design custom-made equipment and to generate specific growth media for the plant cells which may not be available at favorable prices, if at all. Any material problems with the technology underlying our plant cell-based protein expression system may have a material adverse effect on our business, results of operations and financial condition.

The manufacture of our products is an exacting and complex process, and if we or one of our materials suppliers encounter problems manufacturing our products, it will have a material adverse effect on our business and results of operations.

The FDA and foreign regulators require manufacturers to register manufacturing facilities. The FDA and foreign regulators also inspect these facilities to confirm compliance with cGMP or similar requirements that the FDA or foreign regulators establish. We or our materials suppliers may face manufacturing or quality control problems causing product production and shipment delays or a situation where we or the supplier may not be able to maintain compliance with the FDA's cGMP requirements, or those of foreign regulators, necessary to continue manufacturing our drug candidates. Any failure to comply with cGMP requirements or other FDA or foreign regulatory requirements could adversely affect our clinical research activities and our ability to market and develop our products. To date, our current facility has passed audits by the FDA and a number of other regulatory authorities but remains subject to audit by other foreign regulatory authorities. There can be no assurance that we will be able to comply with FDA or foreign regulatory manufacturing requirements for our current facility or any facility we may establish in the future, and the failure to so comply will have a material adverse effect on our business, results of operations and financial condition.

We rely on third parties for final processing of taliglucerase alfa, pegunigalsidase alfa and our product candidates, which exposes us to a number of risks that may delay development, regulatory approval and

commercialization of taliglucerase alfa and our other product candidates or result in higher product costs.

We have no experience in the final filling and freeze drying steps of the drug manufacturing process. We have engaged a European contract manufacturer to act as an additional source of fill and finish activities for taliglucerase alfa and pegunigalsidase alfa, and have engaged other parties for our product candidates. We currently rely primarily on other third-party contractors to perform the final manufacturing steps for taliglucerase alfa on a commercial scale. We may be unable to identify manufacturers and/or replacement manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA and other regulatory authorities, as applicable, must approve any manufacturer and/or replacement manufacturer, including us, and we or any such third party manufacturer might be unable to formulate and manufacture our drug products in the volume and of the quality required to meet our clinical and commercial needs. If we engage any contract manufacturers, such manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical or commercial needs. In addition, contract manufacturers are subject to the rules and regulations of the FDA and comparable foreign regulatory authorities and face the risk that any of those authorities may find that they are not in compliance with applicable regulations. Each of these risks, if realized, could delay our clinical trials, the approval, if any, of taliglucerase alfa and our other potential drug candidates by the FDA and other regulatory authorities, or the commercialization of taliglucerase alfa and our other drug candidates or could result in higher product costs or otherwise deprive us of potential product revenues.

Developments by competitors may render our products or technologies obsolete or non-competitive which would have a material adverse effect on our business, results of operations and financial condition.

We compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Our drug candidates will have to compete with existing therapies and therapies under development by our competitors. In addition, our commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective or safer than our drug products. Other companies have drug candidates in various stages of preclinical or clinical development to treat diseases for which we are also seeking to develop drug products. Some of these potential competing drugs are further advanced in development than our drug candidates and may be commercialized earlier. Even if we are successful in developing effective drugs, our products may not compete successfully with products produced by our competitors. See Business – Competition.

Most of our competitors, either alone or together with their collaborative partners, operate larger research and development programs, staff and facilities and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- undertaking preclinical testing and human clinical trials;
- obtaining marketing approvals from the FDA and other regulatory authorities;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

These organizations also compete with us to attract qualified personnel, acquisitions and joint ventures candidates and for other collaborations. Activities of our competitors may impose unanticipated costs on our business which would have a material adverse effect on our business, results of operations and financial condition.

If we in-license drug candidates, we may delay or otherwise adversely affect the development of our existing drug candidates, which may negatively impact our business, results of operations and financial condition.

In addition to our own internally developed drug candidates, we proactively seek opportunities to in-license and advance other drug candidates that are strategic and have value-creating potential to take advantage of our development know-how and technology. If we in-license any additional drug candidate, our capital requirements may increase significantly. In addition, in-licensing additional drug candidates may place a strain on the time of our existing personnel, which may delay or otherwise adversely affect the development of our existing drug candidates or cause us to re-prioritize our drug pipeline if we do not have the necessary capital resources to develop all of our drug

candidates, which may delay the development of our drug candidates and materially and adversely impact our business, results of operations and financial condition.

If we are unable to manage future growth successfully, there could be a material adverse impact on our business, results of operations and financial condition.

To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability on the part of our management to manage growth could delay the execution of our business plans or disrupt our operations. If we are unable to manage our growth effectively, we may not use our resources in an efficient manner, which may delay the development of our drug candidates and materially and adversely impact our business, results of operations and financial condition.

If we acquire companies, products or technologies, we may face integration risks and costs associated with those acquisitions that could negatively impact our business, results of operations and financial condition.

If we are presented with appropriate opportunities, we may acquire or make investments in complementary companies, products or technologies. We may not realize the anticipated benefit of any acquisition or investment. If we acquire companies or technologies, we will face risks, uncertainties and disruptions associated with the integration process, including difficulties in the integration of the operations of an acquired company, integration of acquired technology with our products, diversion of our management’s attention from other business concerns, the potential loss of key employees or customers of the acquired business and impairment charges if future acquisitions are not as successful as we originally anticipate. In addition, our operating results may suffer because of acquisition-related costs or amortization expenses or charges relating to acquired intangible assets. Any failure to successfully integrate other companies, products or technologies that we may acquire may have a material adverse effect on our business and results of operations. Furthermore, we may have to incur debt or issue equity securities to pay for any additional future acquisitions or investments, the issuance of which could be dilutive to our existing stockholders.

We depend upon key employees and consultants in a competitive market for skilled personnel. If we are unable to attract and retain key personnel, it could adversely affect our ability to develop and market our products.

We are highly dependent upon the principal members of our management team, especially our President and Chief Executive Officer, Moshe Manor, as well as the Chairman of our Board of Directors, Shlomo Yanai, our other directors, our scientific advisory board members, consultants and collaborating scientists. Many of these people have been involved with us for many years and have played integral roles in our progress, and we believe that they will continue to provide value to us. A loss of any of these personnel may have a material adverse effect on aspects of our business, clinical development and regulatory programs. We have employment agreements with Moshe Manor and our other executive officers that may be terminated by us or the applicable officer at any time with varying notice periods of 60 to 90 days. Although these employment agreements generally include non-competition covenants, the applicable noncompetition provisions can be difficult and costly to monitor and enforce. The loss of any of these persons' services may adversely affect our ability to develop and market our products and obtain necessary regulatory approvals. Further, we do not maintain key-man life insurance.

We also depend in part on the continued service of our key scientific personnel and our ability to identify, hire and retain additional personnel, including marketing and sales staff. We experience intense competition for qualified personnel, and the existence of non-competition agreements between prospective employees and their former employers may prevent us from hiring those individuals or subject us to suit from their former employers. While we attempt to provide competitive compensation packages to attract and retain key personnel, many of our competitors are likely to have greater resources and more experience than we have, making it difficult for us to compete successfully for key personnel.

Our collaborations with outside scientists and consultants may be subject to restriction and change.

We work with medical experts, biologists, chemists and other scientists at academic and other institutions, and consultants who assist us in our research, development, regulatory and commercial efforts, including the members of our scientific advisory board. These scientists and consultants have provided, and we expect that they will continue to provide, valuable advice regarding our programs. These scientists and consultants are not our employees, may have other commitments that would limit their future availability to us and typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, we will be unable to prevent them from establishing competing businesses or developing competing products. For example, if a key scientist acting as a principal investigator in any of our clinical trials identifies a potential product or compound that is more scientifically interesting to his or her professional or academic interests, his or her availability to remain involved in our clinical trials could be restricted or eliminated, which may have a material adverse effect on our business, results of operations and financial condition.

Under current U.S. and Israeli law, we may not be able to enforce employees' covenants not to compete and therefore may be unable to prevent our competitors from benefiting from the expertise of some of our former employees.

We have entered into non-competition agreements with substantially all of our employees. These agreements prohibit our employees, if they cease working for us, from competing directly with us or working for our competitors for a limited period. Under current U.S. and Israeli law, we may be unable to enforce these agreements against most of our employees and it may be difficult for us to restrict our competitors from gaining the expertise our former employees gained while working for us. If we cannot enforce our employees' non-compete agreements, we may be unable to prevent our competitors from benefiting from the expertise of our former employees, which may have a material adverse effect on our business, results of operations and financial condition.

Our internal computer systems, or those used by our third-party contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our present and future contractors and consultants are vulnerable to damage from computer viruses and unauthorized access. Although to our knowledge we have not experienced any material system failure 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. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates and to 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.

If product liability claims are brought against us, it may result in reduced demand for our products and product candidates or damages that exceed our insurance coverage.

The clinical testing, marketing and use of our products and product candidates exposes us to product liability claims if the use or misuse of those products or product candidates cause injury or disease, or results in adverse effects. Use of our products or product candidates, whether in clinical trials or post approval, could result in product liability claims. We presently carry clinical trial liability insurance with coverages of up to $10.0 million per occurrence and $10.0 million in the aggregate, an amount we consider reasonable and customary. However, this insurance coverage includes various deductibles, limitations and exclusions from coverage, and in any event might not fully cover any potential claims. We may need to obtain additional clinical trial liability coverage prior to initiating additional clinical trials. We expect to obtain product liability insurance coverage before commercialization of our product candidates; however, such insurance is expensive and insurance companies may not issue this type of insurance when we need it. We may not be able to obtain adequate insurance in the future at an acceptable cost. Any product liability claim, even one that was not in excess of our insurance coverage or one that is meritless and/or unsuccessful, may adversely affect our cash available for other purposes, such as research and development, which may have a material adverse effect on our business, results of operations and financial condition. Product liability claims, even if without merit, may result in reduced demand for our products, if approved, which would have a material adverse effect on our business, results of operations and financial condition. In addition, the existence of a product liability claim could affect the market price of our common stock.

Reforms in the healthcare industry and the uncertainty associated with pharmaceutical pricing, reimbursement and related matters could adversely affect the marketing, pricing and demand for our products, if approved.

Increasing healthcare expenditures have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would result in changes in the U.S. healthcare system have been introduced or proposed in the U.S. Congress and in some state legislatures within the United States, including reductions in the pricing of prescription products and changes in the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products. Legislation passed in recent years has imposed certain changes to the way in which drugs, including our product candidates, are covered and reimbursed in the United States. For example, federal legislation and regulations have implemented new reimbursement methodologies for certain drugs, created a voluntary prescription drug benefit, Medicare Part D, and have imposed significant revisions to the Medicaid Drug Rebate Program. The PPACA imposes yet additional changes to these programs. We believe that legislation that reduces reimbursement for our product candidates could adversely impact how much or under what circumstances healthcare providers will prescribe or administer our product candidates, if approved. This could materially and adversely impact our business by reducing our ability to generate revenue, raise capital, obtain additional collaborators and market our products, if approved. In addition, we believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of pharmaceutical products, which may adversely impact product sales, upon approval, if at all.

Governments outside the United States tend to impose strict price controls and reimbursement approval policies, which may adversely affect our prospects for generating revenue.

In some countries, particularly European Union member states, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time (six to 12 months or longer) after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries with respect to any product candidate that achieves regulatory approval, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products upon approval, if at all, is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our prospects for generating revenue, if any, could be adversely affected which would have a material adverse effect on our business, results of operations and financial condition. Further, if we achieve regulatory approval of any product, we must successfully negotiate product pricing for such product in individual countries. As a result, the pricing of our product candidates, if approved, in different countries may vary widely, thus creating the potential for third-party trade in our products in an attempt to exploit price differences between countries. This third-party trade of our products could undermine our sales in markets with higher prices which could have a material adverse effect on our business, results of operations and financial condition.

Our ability to utilize net operating loss carryforwards may be limited.

Our NOLs, as of December 31, 2017, are equal to approximately $207 million, of which approximately $23 million may be restricted under Section 382 of the Internal Revenue Code of 1986, as amended, or the “Code.” Section 382 of the Code imposes limitations on a corporation’s ability to utilize NOLs to offset taxable income if the corporation experiences an “ownership change.” In general terms, an “ownership change” may result from transactions increasing the ownership of certain stockholders in the stock of a corporation by more than 50% over a three-year period. In the event that an ownership change has occurred (including as a result of conversion of our outstanding convertible notes into shares of our common stock), or were to occur, utilization of our NOLs would be subject to an annual limitation under Section 382, which is generally the fair market value of the pre-change entity multiplied by the long-term tax exempt rate, which is published monthly by the U.S. Internal Revenue Service.

Our corporate structure may create U.S. federal income tax inefficiencies

Protalix Ltd. is our wholly-owned subsidiary and thus a controlled foreign corporation of our company for U.S. federal income tax purposes. This organizational structure may create inefficiencies, as certain types of income and investments of Protalix Ltd. that otherwise would not be currently taxable under general U.S. federal income tax principles may become taxable. These inefficiencies may require us to use more of our NOLs than we otherwise might and may result in a tax liability without a corresponding distribution from our subsidiary.

We are a holding company with no operations of our own.

We are a holding company with no operations of our own. Accordingly, our ability to conduct our operations, service any debt that we may incur in the future and pay dividends, if any, is dependent upon the earnings from the business conducted by Protalix Ltd. The distribution of those earnings or advances or other distributions of funds by our subsidiary to us, as well as our receipt of such funds, are contingent upon the earnings of Protalix Ltd. and are subject to various business considerations and U.S. and Israeli law. If Protalix Ltd. is unable to make sufficient distributions or advances to us, or if there are limitations on our ability to receive such distributions or advances, we may not have the cash resources necessary to conduct our corporate operations or service our debt which would have a material adverse effect on our business, results of operations and financial condition.

Risks Related to Our Financial Condition and Capital Requirements

Servicing our debt and settling conversion requests may require a significant amount of cash, and we may not have sufficient cash flow from our business to pay our debt. Furthermore, restrictive covenants governing our indebtedness may restrict our ability to raise additional capital.

Our ability to pay interest on, or to make any scheduled or otherwise required payment of the principal of, and settle conversion requests on our outstanding convertible notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt and make necessary expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. If we raise additional debt, it would increase our interest expense, leverage and operating and financial costs. In addition, the terms of the indentures governing our outstanding convertible notes, which are secured by certain of our material assets, including all of our intellectual property, and the agreements governing future indebtedness may restrict us from adopting any of these alternatives. We may be able to obtain amendments and waivers of such restrictions, subject to such restrictions under the terms of the applicable indenture or any subsequent indebtedness. In the event of any such default, the holders of the indebtedness could, among other things, elect to declare all amounts owed immediately due and payable, which could cause all or a large portion of our available cash flow to be used to pay such amounts and thereby reduce the amount of cash available to pursue our business plans or force us into bankruptcy or liquidation, or, with respect to our indebtedness that is secured, result in the foreclosure on the assets that secure the debt, which would force us to relinquish rights to assets that we may believe are critical to our business. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Any default on our debt will have a material adverse effect on our business, results of operations and financial condition.

A substantial majority of our authorized shares of common stock under our certificate of incorporation are either outstanding or reserved for issuance.

Our certificate of incorporation currently authorizes the issuance of 250,000,000 shares of common stock and 100,000,000 shares of preferred stock, par value $0.0001 per share, for a total of 350,000,000 shares of capital stock. As of December 31, 2017, a total of approximately 4.9 million shares of common stock are reserved for issuance upon the exercise of outstanding stock options under our 2006 Stock Incentive Plan, as amended, and a total of 2,554,075 shares of common stock are reserved for issuance in connection with future grants of stock options and/or future issuances of shares under the plan. In addition, approximately 81.6 million shares of common stock are reserved for issuance upon the conversion of our outstanding convertible notes. After taking into account the total number of shares of common stock issued and outstanding, in addition to the aggregate number of shares of common stock reserved for future issuance as described above, approximately 6.9% of our authorized shares of common stock

remain available to be issued or reserved for issuance as of the date of this report.

We currently intend to solicit the approval of our stockholders at our upcoming 2018 annual meeting of stockholders to increase the number of authorized shares. Absent the approval, we are left without sufficient, authorized shares of common stock to pursue a variety of other business and financial objectives without further action of the stockholders (except when required by applicable law or regulation). As a result, a delay in securing, or a failure to secure, stockholder approval to amend our certificate of incorporation would seriously jeopardize the financial viability of the Company. Unless and until we attain the approval of our stockholders to increase the number of authorized shares, our ability to manage our capital needs is restricted which may have a material adverse effect on our business, results of operations and financial condition.

Our significant level of indebtedness could adversely affect our business, results of operations and financial condition and prevent us from fulfilling our obligations under our convertible notes and our other indebtedness.

Our outstanding convertible notes represent a significant amount of indebtedness with substantial debt service requirements. We may also incur additional indebtedness to meet future financing needs. Our substantial indebtedness could have material adverse effects on our business, results of operations and financial condition. For example, it could:

- make it more difficult for us to satisfy our financial obligations, including with respect to the convertible notes;
- result in an event of default under our outstanding convertible notes if we fail to comply with the financial and other restrictive covenants contained in agreements governing any future indebtedness, which event of default could result in all of our debt becoming immediately due and payable;
- increase our vulnerability to general adverse economic, industry and competitive conditions;
- reduce the availability of our cash flow to fund working capital, capital expenditures, acquisitions and other general corporate purposes because we will be required to dedicate a substantial portion of our cash flow from operations to the payment of principal and interest on our indebtedness;

- limit our flexibility in planning for, or reacting to, and increasing our vulnerability to changes in our business, the industry in which we operate and the general economy;
- prevent us from raising funds necessary to purchase convertible notes surrendered to us by holders upon a fundamental change (as described in the indentures governing the two series of convertible notes), which failure would result in an event of default with respect to the convertible notes;
- place us at a competitive disadvantage compared to our competitors that have less indebtedness or are less highly leveraged and that, therefore, may be able to take advantage of opportunities that our debt levels or leverage prevent us from exploiting; and
- limit our ability to obtain additional financing.

Each of these factors may have a material and adverse effect on our business, results of operations and financial condition and our ability to meet our payment obligations under the convertible notes and our other indebtedness. Our ability to make payments with respect to the convertible notes and to satisfy any other debt obligations depends on our future operating performance and our ability to generate significant cash flow in the future, which will be affected by prevailing economic conditions and financial, business, competitive, legislative and regulatory factors as well as other factors affecting our company and industry, many of which are beyond our control.

If we are unable to refinance or otherwise defease the remaining outstanding 4.5% convertible notes on or prior to June 16, 2018, we may face liquidity constraints.

If we are not able to refinance or otherwise defease all of our outstanding 4.5% convertible notes by June 16, 2018, the maturity date of the 7.5% convertible notes will be accelerated to June 15, 2018. Our ability to refinance or retire our outstanding 4.5% convertible notes will depend on our cash balance, the capital markets environment and our financial condition as well as the terms of the indenture governing the 7.5% convertible notes. The indenture governing the 7.5% convertible notes includes certain payment restrictions that may limit our ability to defease the 4.5% convertible notes. If the maturity of the 7.5% convertible notes is accelerated, we may be unable to obtain financing to pay the principal amount thereof, which will have a material adverse effect on our business, results of operations and financial condition.

We are required to comply with a number of covenants under the indenture governing our outstanding 7.5% convertible notes that could hinder our growth.

The indenture governing our 7.5% convertible notes contains a number of restrictive affirmative and negative covenants, which limit our ability to incur additional debt; exceed certain limits; pay dividends or distributions; or merge, consolidate or dispose of substantially all of our assets, including all of our intellectual property assets and other material assets securing such convertible notes. A breach of these covenants could result in default, and if such default is not cured or waived, the holders of the indebtedness could, among other things, elect to declare all amounts owed immediately due and payable, which could cause all or a large portion of our available cash flow to be used to

pay such amounts and thereby reduce the amount of cash available to pursue our business plans or force us into bankruptcy or liquidation, or, result in the foreclosure on the assets that secure the debt, including all of our intellectual property assets, which would force us to relinquish rights to such assets that we may believe are critical to our business. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Any default on our debt will have a material adverse effect on our business, results of operations and financial condition.

Any conversion of our outstanding convertible notes into common stock will dilute the ownership interest of our existing stockholders, including holders who had previously converted their notes.

The conversion of some or all of our convertible notes into shares of our common stock will dilute the ownership interests of our existing stockholders. Any sales in the public market of our common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of our outstanding convertible notes may encourage short selling by market participants because the conversion of convertible notes could depress the market price of our common stock.

The fundamental change purchase feature of our outstanding convertible notes may delay or prevent an otherwise beneficial attempt to take over our company.

The terms of our outstanding convertible notes require us to offer to purchase the notes for cash in the event of a fundamental change. A non-stock takeover of our company may trigger the requirement that we purchase the notes. This feature may have the effect of delaying or preventing a takeover of our company that would otherwise be beneficial to our stockholders.

We may fail to meet the continued market capitalization-based listing requirement or other continued listing requirements of The NYSE American.

The stock market in general, and the market for life sciences companies in particular, have experienced extreme price and volume fluctuations that may have been unrelated or disproportionate to the operating performance of the listed companies. There have been dramatic fluctuations in the market prices of securities of biotechnology companies. These price fluctuations may be rapid and severe and may leave investors little time to react. Broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. Sharp drops in the market price of our common stock expose us to securities class-action litigation. The trading price of our common stock has been volatile and has been subject to wide price fluctuations in response to various factors, many of which are beyond our control. The volatility of our stock price has from time to time in recent periods affected our market capitalization. Stock price fluctuations that adversely affect our market capitalization may result in a failure to meet the continued market capitalization-based listing requirement for The NYSE American, which would require us to take steps to gain compliance with alternate listing standards or take remedial steps to bring us into compliance. A failure to maintain or regain compliance with applicable listing standards could adversely affect the liquidity of our common stock.

We currently have no significant product revenues and may need to raise additional capital to operate our business, which may not be available on favorable terms, or at all, and which will have a dilutive effect on our stockholders.

To date, we have not generated significant revenues from product sales and only minimal revenues from research and development services and other fees, other than the milestone and other payments we have received in connection with our agreements with Pfizer and Chiesi. For the years ended December 31, 2017, 2016 and 2015, we had net losses from continuing operations of $47.3 million, excluding a one-time, non-cash net charge of $38 million in connection with the remeasurement of a derivative, $29.2 million and $27.3 million, respectively, primarily as a result of expenses incurred through a combination of research and development activities and expenses supporting those activities, which includes share-based compensation expense. Drug development and commercialization is very capital intensive. We fund all of our operations and capital expenditures from the revenues we generate from licensing

fees and grants, the net proceeds of equity and debt offerings and other sources. Based on our current plans, expectations and capital resources, we believe that our cash and cash equivalents will be sufficient to enable us to meet our planned operating needs for at least 12 months. However, changes may occur that could consume our existing capital at a faster rate than projected, including, among others, the cost and timing of regulatory approvals, changes in the progress of our research and development efforts and the costs of protecting our intellectual property rights.

We may need to finance our future cash needs through corporate collaboration, licensing or similar arrangements, public or private equity offerings or debt financings. If we are unable to secure additional financing in the future on acceptable terms, or at all, we may be unable to commence or complete planned preclinical and clinical trials or obtain approval of our drug candidates from the FDA and other regulatory authorities. In addition, we may be forced to reduce or discontinue product development or product licensing, reduce or forego sales and marketing efforts and other commercialization activities or forego attractive business opportunities in order to improve our liquidity and to enable us to continue operations which would have a material adverse effect on our business and results of operations. Furthermore, any additional source of financing will likely involve the issuance of our equity securities, which will have a dilutive effect on our stockholders. See also "—A substantial majority of our authorized shares of common stock under our certificate of incorporation are either outstanding or reserved for issuance."

We are not currently profitable and delays in achieving profitability, if at all, will have a material adverse effect on our business and results of operations and could negatively impact the value of our common stock.

We may incur losses for the foreseeable future. We expect to continue to incur significant operating expenditures, and we anticipate that our expenses will increase in the foreseeable future as we:

- continue to undertake preclinical development and clinical trials for our current and new drug candidates;
- seek regulatory approvals for our drug candidates; and
- seek to license-in additional technologies.

We also may continue to experience negative cash flow for the foreseeable future as we fund our operating losses and capital expenditures. As a result, we will need to generate significant revenues in order to achieve and maintain profitability. We may not be able to generate these revenues or achieve profitability in the foreseeable future, if at all. Delays in achieving profitability, or subsequent failures to maintain profitability, will have a material adverse effect on our business and results of operations and could negatively impact the value of our common stock.

Risks Related to Investing in our Common Stock

The market price of our common stock may fluctuate significantly.

The market price of our common stock may fluctuate significantly in response to numerous factors, some of which are beyond our control, such as:

- the progress and results of our ongoing studies regarding pegunigalsidase alfa and our other product candidates;
- announcements regarding partnerships or collaborations by us or our competitors;
- purchases of alfataliglicerase in Brazil;
- developments concerning intellectual property rights and regulatory approvals;
- the announcement of new products or product enhancements by us or our competitors;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts;
- developments in the biotechnology industry; and
- general market conditions and other factors, including factors unrelated to our operating performance.

Further, stock markets in general, and the market for biotechnology companies in particular, have recently experienced price and volume fluctuations. Continued market fluctuations could result in extreme volatility in the price of our common stock, which could cause a decline in the value of our common stock. Price volatility of our common stock may be worse if the trading volume of our common stock is low. We have not paid, and do not expect to pay, any cash dividends on our common stock as any earnings generated from future operations will be used to finance our operations. As a result, investors will not realize any income from an investment in our common stock until and unless their shares are sold at a profit.

Future sales of our common stock could reduce our stock price.

If our existing stockholders or their distributees sell substantial amounts of our common stock in the public market, including shares of our common stock issuable upon conversion of our outstanding convertible notes, the market price of our common stock could decrease significantly. The perception in the public market that our existing stockholders might sell shares of common stock could also depress the trading price of our common stock. Any such sales of our common stock in the public market may affect the price of our common stock.

A substantial majority of our outstanding shares of our common stock are freely tradable without restriction or further registration under the federal securities laws, unless owned by our affiliates. In addition, we may sell additional shares of our common stock in the future to raise capital and a substantial number of shares of our common stock are reserved for issuance upon the exercise of stock options and upon conversion of our outstanding convertible notes. We cannot predict the size of future issuances, if any. At December 31, 2017, there were outstanding options to purchase common stock issued covering approximately 4.9 million shares of our common stock with a weighted average exercise price of $3.59 per share. Also at December 31, 2017, there were approximately 2.6 million shares of common stock available for future for issuance in connection with future grants of incentives under our amended 2006 stock incentive plan and approximately 81.1 million shares of common stock reserved for issuance upon conversion of our outstanding convertible notes. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities.

If securities analysts stop publishing research or reports about us or our business or if they downgrade our common stock, the market price of our common stock could decline.

The market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. We do not control these analysts. If any analyst who covers us downgrades our stock or lowers its future stock price targets or estimates of our operating results, the market price for our common stock could decline rapidly. Furthermore, if any analyst ceases to cover us, we could lose visibility in the market, which in turn could cause the market price of our common stock to decline.

Our common stock is listed to trade on more than one stock exchange, and this may result in price variations.

Our common stock is listed for trade on both the NYSE American and the TASE. Dual-listing may result in price variations between the exchanges due to a number of factors. First, our common stock is traded in U.S. dollars on the NYSE American and in NIS on the TASE. In addition, the exchanges are open for trade at different times of the day and on different days. For example, the TASE opens generally during Israeli business hours, Sunday through Thursday, while the NYSE American opens generally during U.S. business hours, Monday through Friday. The two exchanges also have differing vacation schedules. Differences in the trading schedules, as well as volatility in the exchange rate of the two currencies, among other factors, may result different trading prices for our common stock on the two exchanges. Other external influences may have different effects on the trading price of our common stock on the two exchanges.

Directors and executive officers own a significant percentage of our capital stock, and they may make decisions that an investor may not consider to be in the best interests of our stockholders.

Our directors and executive officers, principal stockholders and affiliated entities beneficially own, in the aggregate, approximately 4.0% of our common stock, as of February 15, 2018, giving effect to stock options that are held by such persons that are exercisable within such 60 days from such date. As a result, if some or all of them acted together, they would have the ability to exert substantial influence over the election of our Board of Directors and the outcome of issues requiring approval by our stockholders. This concentration of ownership may have the effect of delaying or preventing a change in control of our company that may be favored by other stockholders. This could prevent the consummation of transactions favorable to other stockholders, such as a transaction in which stockholders might otherwise receive a premium for their shares over current market prices.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and operating results. In addition, current and potential

stockholders could lose confidence in our financial reporting, which could have a material adverse effect on the price of our common stock.

Effective internal controls are necessary for us to provide reliable financial reports and effectively prevent fraud. If we cannot provide reliable financial reports or prevent fraud, our results of operation could be harmed.

Section 404 of the Sarbanes-Oxley Act of 2002 requires annual management assessments of the effectiveness of our internal controls over financial reporting and a report by our independent registered public accounting firm addressing these assessments. We continuously monitor our existing internal controls over financial reporting systems to confirm that they are compliant with Section 404, and we may identify deficiencies that we may not be able to remediate in time to meet the deadlines imposed by the Sarbanes-Oxley Act. This process may divert internal resources and will take a significant amount of time and effort to complete.

If, at any time, it is determined that we are not in compliance with Section 404, we may be required to implement new internal control procedures and reevaluate our financial reporting. We may experience higher than anticipated operating expenses as well as increased independent auditor fees during the implementation of these changes and thereafter. Further, we may need to hire additional qualified personnel. If we fail to maintain the adequacy of our internal controls, as such standards are modified, supplemented or amended from time to time, we may not be able to conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act, which could result in our being unable to obtain an unqualified report on internal controls from our independent auditors. Failure to maintain an effective internal control environment could also cause investors to lose confidence in our reported financial information, which could have a material adverse effect on the price of our common stock.

Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses, divert management's attention from operating our business which could have a material adverse effect on our business.

There have been other changing laws, regulations and standards relating to corporate governance and public disclosure in addition to the Sarbanes-Oxley Act, as well as new regulations promulgated by the Commission and rules promulgated by the national securities exchanges, including the NYSE American and the NASDAQ. These new or changed laws, regulations and standards are subject to varying interpretations in many cases due to their lack of specificity, and as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. As a result, our efforts to comply with evolving laws, regulations and standards are likely to continue to result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities. Our board members, Chief Executive Officer and Chief Financial Officer could face an increased risk of personal liability in connection with the performance of their duties. As a result, we may have difficulty attracting and retaining qualified board members and executive officers, which could have a material adverse effect on our business. If our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, we may incur additional expenses to comply with standards set by regulatory authorities or governing bodies which would have a material adverse effect on our business, results of operations and financial condition.

The issuance of preferred stock or additional shares of common stock could adversely affect the rights of the holders of shares of our common stock.

Our Board of Directors is authorized to issue up to 100,000,000 shares of preferred stock without any further action on the part of our stockholders. Our Board of Directors has the authority to fix and determine the voting rights, rights of redemption and other rights and preferences of preferred stock. Currently, we have no shares of preferred stock outstanding.

Our Board of Directors may, at any time, authorize the issuance of a series of preferred stock that would grant to holders the preferred right to our assets upon liquidation, the right to receive dividend payments before dividends are distributed to the holders of common stock and the right to the redemption of the shares, together with a premium, before the redemption of our common stock, which may have a material adverse effect on the rights of the holders of our common stock. In addition, our Board of Directors, without further stockholder approval, may, at any time, issue large blocks of preferred stock. In addition, the ability of our Board of Directors to issue shares of preferred stock without any further action on the part of our stockholders may impede a takeover of our company and may prevent a transaction that is favorable to our stockholders.

Under the rules of the TASE, other than incentives under our amended 2006 stock incentive plan, we were prohibited from issuing any securities of any class or series different than the common stock that is listed on the TASE for the 12-month period immediately succeeding our initial listing, which occurred on September 6, 2010. As of the date hereof, the rules of the TASE allow us to issue securities with preferential rights with respect to dividends but such other securities may not include voting rights. The foregoing does not limit our liability to issue and grant options and warrants for the purchase of shares of our common stock.

Risks Related to the Commercialization of Drug Products

Fiocruz may not comply with the terms and conditions of the Supply and Technology Transfer Agreement.

We do not control and may not be able to effectively influence Fiocruz's ability to distribute alfataliglicerase in Brazil. If Fiocruz fails to comply with the purchase requirements of the Supply and Technology Transfer Agreement, we may terminate the agreement and market alfataliglicerase in Brazil on our own. Any failure by Fiocruz to comply with the purchase requirements of the Supply and Technology Transfer Agreement, or any other material breach by Fiocruz of the agreement, may have a material adverse effect on our business, results of operations and financial condition.

In 2017, we received a purchase order from the Brazilian MoH for the purchase of approximately $24.3 million of alfataliglicerase for the treatment of Gaucher patients in Brazil. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in the best interest of our company.

We face the risk that the Brazilian MoH may ultimately fail to purchase the amounts of alfataliglicerase for which it has already stated its intentions. In addition, we may fail to supply the intended amounts on time, if at all. We also cannot accurately predict the amount of revenues we will generate under our Supply and Technology Transfer with Fiocruz in future periods, if any. Any failure by the Brazilian MoH to purchase alfataliglicerase, by us, to supply alfataliglicerase for purchase or by Fiocruz to distribute alfataliglicerase in Brazil, or the experience of significant delays in any of the foregoing, may have a material adverse effect on our business, results of operations and financial condition.

We have limited experience in selling, marketing or distributing products and limited internal capability to do so.

We currently have very limited sales, marketing or distribution capabilities and no experience in building a sales force and distribution capabilities. We retained the marketing rights to alfataliglicerase in Brazil and, under the Chiesi Agreement, we retained the rights to market pegunigalsidase alfa in the United States, if approved. We have not licensed the marketing or commercialization rights to any of our other product candidates to any party. The commercialization of a drug product requires that we commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and with supporting distribution capabilities. Factors that may inhibit our efforts to commercialize our products directly and without strategic partners include:

- the inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to an adequate numbers of physicians or to pursuance them to prescribe our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating and sustaining an independent sales and marketing organization.

We may not be successful in recruiting or retaining the sales and marketing personnel necessary to sell alfataliglicerase or any of our products upon approval, if at all, which would have a material adverse effect on our

business, results of operations and financial condition.

We may enter into distribution arrangements and marketing alliances for certain products and any failure to successfully identify and implement these arrangements on favorable terms, if at all, may impair our ability to commercialize our product candidates.

We may need to establish a sales force to market alfataliglicerase or our our product candidates, if approved. We do not anticipate having the resources in the foreseeable future to develop global sales and marketing capabilities for all of the products we are developing. We may elect to pursue arrangements regarding the sales and marketing and distribution of alfataliglicerase or one or more of our product candidates, and our future revenues may depend, in part, on our ability to enter into and maintain arrangements with other companies having sales, marketing and distribution capabilities and the ability of such companies to successfully market and sell any such products. Any failure to enter into such arrangements and marketing alliances on favorable terms, if at all, could delay or impair our ability to commercialize our product candidates and could increase our costs of commercialization. Any use of distribution arrangements and marketing alliances to commercialize our product candidates will subject us to a number of risks, including the following:

- we may be required to relinquish important rights to our products or product candidates;
- we may not be able to control the amount and timing of resources that our distributors or collaborators may devote to the commercialization of our product candidates;
- our distributors or collaborators may experience financial difficulties;
- our distributors or collaborators may not devote sufficient time to the marketing and sales of our products; and
- business combinations or significant changes in a collaborator's business strategy may adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement.

We may need to enter into additional co-promotion arrangements with third parties where our own sales force is neither well situated nor large enough to achieve maximum penetration in the market. We may not be successful in entering into any co-promotion arrangements, and the terms of any co-promotion arrangements we enter into may not be favorable to us.

If physicians, patients, third party payors and others in the medical community do not accept and use taliglucerase alfa, or any of our other product candidates, if approved, our ability to generate revenue from product sales will be materially impaired.

Physicians and patients, and other healthcare providers, may not accept and use any of our products or any product candidates, if approved, for marketing. Future acceptance and use of any of our products or any product candidates, if approved, will depend upon a number of factors including:

- perceptions by physicians, patients, third party payors and others in the medical community about the safety and effectiveness of taliglucerase alfa or our other drug candidates;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the prevalence and severity of any side effects, including any limitations or warnings contained in our products' approved labeling;
- pharmacological benefits of taliglucerase alfa or our other drug candidates relative to competing products and products under development;
- the efficacy and potential advantages relative to competing products and products under development;
- relative convenience and ease of administration;
- effectiveness of education, marketing and distribution efforts by us and our licensees and distributors, if any;
- publicity concerning taliglucerase alfa or our other drug candidates or competing products and treatments;
- coverage and reimbursement of our products by third party payors; and
- the price for our products and competing products.

A lack of market acceptance of taliglucerase alfa in Brazil, or globally for any of our other products candidates, if approved, would have a material adverse effect on our business, results of operations and financial condition.

If the market opportunities for other product candidates, and for taliglucerase alfa in Brazil, are smaller than we believe they are, our revenues may be adversely affected and our business may suffer.

To date, our development efforts have focused mainly on relatively rare disorders with small patient populations, in particular Gaucher disease and Fabry disease. Currently, most reported estimates of the prevalence of these diseases are based on studies of small subsets of the population of specific geographic areas, which are then extrapolated to estimate the prevalence of the diseases in the broader world population. As new studies are performed, the estimated prevalence of these diseases may change. There can be no assurance that the prevalence of Gaucher disease or Fabry disease in the study populations, particularly in these newer studies, accurately reflect the prevalence of these diseases in the broader world population. If the market opportunities for our current product candidates are smaller than we believe they are, our revenues may be adversely affected and our business may suffer.

Coverage and reimbursement may not be available for alfataliglicerase or any of our other product candidates, if approved, in all territories which could diminish our sales or affect our ability to sell alfataliglicerase or any other products profitably.

Market acceptance and sales of alfataliglicerase in Brazil, or for any of our other product candidates globally, if approved, will depend on coverage and reimbursement policies in the countries in which they are approved for sale. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Obtaining reimbursement approval for an approved product from governments and other third party payors is a time consuming and costly process that requires our collaborators or us, as the case may be, to provide supporting scientific, clinical and cost-effectiveness data for the use of our products, if and when approved, to every payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement or we might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of approved products, if any, to such payors' satisfaction. Such studies might require our collaborators or us to commit a significant amount of management time and financial and other resources. Even if a payor determines that an approved product is eligible for reimbursement, the payor may impose coverage limitations that preclude payment for some uses that are approved by the FDA or other regulatory authorities. In addition, full reimbursement may not be available for high priced products. Moreover, eligibility for coverage does not imply that any approved product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Also, limited reimbursement amounts may reduce the demand for, or the price of, our product candidates. Except with respect to taliglucerase alfa, we have not commenced efforts to have our product candidates covered and reimbursed by government or third-party payors. If coverage and reimbursement are not available or are available only to limited levels, the sales of our products, if approved may be diminished or we may not be able to sell such products profitably.

We and our collaborating partners may be subject, directly or indirectly, to federal and state healthcare fraud and abuse and false claims laws and regulations. If we or our collaborating partners are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

All marketing activities associated with drug products that are approved for sale in the United States, if any, will be, directly or indirectly through our customers, subject to numerous federal and state laws governing the marketing and promotion of pharmaceutical products in the United States, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act and HIPAA. These laws may adversely impact, among other things, our proposed sales, marketing and education programs.

The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit

arrangements, payments of cash, waivers of co-payments and deductibles, ownership interests and providing anything at less than its fair market value. The reach of the Anti-Kickback Statute was also broadened by the PPACA which, among other things, amends the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b, effective March 23, 2010. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that 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 civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. The federal Anti-Kickback Statute is broad, and despite a series of narrow safe harbors, prohibits many arrangements and practices that are lawful in businesses outside of the healthcare industry. Penalties for violations of the federal Anti-Kickback Statute include criminal penalties and civil sanctions such as fines, imprisonment and possible exclusion from Medicare, Medicaid and other state or federal healthcare programs. Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs, and do not contain identical safe harbors.

The federal False Claims Act imposes liability on any person who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The "qui tam" provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payer and not merely a federal healthcare program. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties of $5,500 to $11,000 for each separate false claim.

HIPAA created several new federal crimes, including health care fraud, and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private third-party payers. The false statements statute prohibits 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 health care benefits, items or services.

We are unable to predict whether we could be subject to actions under any of these or other fraud and abuse laws, or the impact of such actions. Moreover, to the extent that taliglucerase alfa, or any of our products, if approved for marketing, will be sold in a foreign country, we and our future collaborators, may be subject to similar foreign laws and regulations. If we or any of our future collaborators are found to be in violation of any of the laws described above and other applicable state and federal fraud and abuse laws, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare reimbursement programs and the curtailment or restructuring or our operations, any of which could have a material adverse effect on our business, results of operations and financial condition.

Risks Related to Intellectual Property Matters

The intellectual property and assets owned by our subsidiaries are subject to security agreements that secure our payment and other obligations under our 7.5% convertible notes, and our subsidiaries have guaranteed all of those obligations.

In connection with the issuance of our 7.5% convertible notes, we entered into security agreements pursuant to which our subsidiaries provided first priority security interests in all of their assets, which consist of all of our intellectual property and other material assets. The security agreements secure certain payment, indemnification and other obligations under the 7.5% convertible notes. If we were to default on certain of ours obligations, or in certain other circumstances generally related to a bankruptcy or insolvency, holders of our outstanding 7.5% convertible notes could seek to foreclose on the collateral under the security agreements to obtain satisfaction our obligations, and our business could be materially and adversely impacted, which would in turn materially and adversely impact our

business, results of operations and financial condition.

Furthermore, in connection with the issuance of the 7.5% convertible notes, our subsidiaries guaranteed all of our obligations under the indenture governing such convertible notes. If we were to default on our obligations under the indenture, the holders could require our subsidiaries to satisfy all of those obligations under the guarantees.

If we fail to adequately protect or enforce our intellectual property rights or secure rights to third party patents, the value of our intellectual property rights would diminish and our business, competitive position and results of operations would suffer.

As of December 31, 2017, we had 58 pending patent applications of which eight are joint pending patent applications with a third party and one is an-in licensed application. However, the filing of a patent application does not mean that we will be issued a patent, or that any patent eventually issued will be as broad as requested in the patent application or sufficient to protect our technology. Any modification required to a current patent application may delay the approval of such patent application which would have a material adverse effect on our business, results of operations and financial condition. In addition, there are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications to not be granted, including known or unknown prior art, deficiencies in the patent application or the lack of originality of the technology. Our competitive position and future revenues will depend in part on our ability and the ability of our licensors and collaborators to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing the proprietary rights of third parties. We have filed U.S. and international patent applications for process patents, as well as composition of matter patents, for taliglucerase alfa and other product candidates. However, we cannot predict:

- the degree and range of protection any patents will afford us against competitors and those who infringe upon our patents, including whether third parties will find ways to invalidate or otherwise circumvent our licensed patents;
- if and when patents will issue;
- whether or not others will obtain patents claiming aspects similar to those covered by our licensed patents and patent applications; or
- whether we will need to initiate litigation or administrative proceedings, which may be costly, and whether we win or lose.

As of December 31, 2017, we held, or had license rights to, 69 patents. If patent rights covering our products or technologies are not sufficiently broad, they may not provide us with sufficient proprietary protection or competitive advantages against competitors with similar products and technologies. Furthermore, if the U.S. Patent and Trademark Office or foreign patent offices issue patents to us or our licensors, others may challenge the patents or circumvent the patents, or the patent office or the courts may invalidate the patents. Thus, any patents we own or license from or to third parties may not provide any protection against our competitors and those who infringe upon our patents.

Furthermore, the life of our patents is limited. The patents we hold, and the patents that may be issued in the future based on patent applications from the patent families, relating to our ProCellEx protein expression system are expected to expire between 2017 and 2025.

We rely on confidentiality agreements that could be breached and may be difficult to enforce which could have a material adverse effect on our business and competitive position.

Our policy is to enter agreements relating to the non-disclosure of confidential information with third parties, including our contractors, consultants, advisors and research collaborators, as well as agreements that purport to require the disclosure and assignment to us of the rights to the ideas, developments, discoveries and inventions of our employees and consultants while we employ them. However, these agreements can be difficult and costly to enforce. Moreover, to the extent that our contractors, consultants, advisors and research collaborators apply or independently develop intellectual property in connection with any of our projects, disputes may arise as to the proprietary rights to the intellectual property. If a dispute arises, a court may determine that the right belongs to a third party, and enforcement of our rights can be costly and unpredictable. In addition, we rely on trade secrets and proprietary know-how that we seek to protect in part by confidentiality agreements with our employees, contractors, consultants, advisors and others. Despite the protective measures we employ, we still face the risk that:

- these agreements may be breached;
- these agreements may not provide adequate remedies for the applicable type of breach; or
- our trade secrets or proprietary know-how will otherwise become known.

Any breach of our confidentiality agreements or our failure to effectively enforce such agreements may have a material adverse effect on our business and competitive position.

If we infringe the rights of third parties we could be prevented from selling products, forced to pay damages and required to defend against litigation which could result in substantial costs and may have a material adverse effect on our business, results of operations and financial condition.

We have not received to date any claims of infringement by any third parties. However, as our drug candidates progress into clinical trials and commercialization, if at all, our public profile and that of our drug candidates may be raised and generate such claims. Defending against such claims, and occurrence of a judgment adverse to us, could result in unanticipated costs and may have a material adverse effect on our business and competitive position. If our products, methods, processes and other technologies infringe the proprietary rights of other parties, we may incur substantial costs and we may have to:

- obtain licenses, which may not be available on commercially reasonable terms, if at all;
- redesign our products or processes to avoid infringement;
- stop using the subject matter claimed in the patents held by others, which could cause us to lose the use of one or more of our drug candidates;
- defend litigation or administrative proceedings that may be costly whether we win or lose, and which could result in a substantial diversion of management resources; or
- pay damages.

Any costs incurred in connection with such events or the inability to sell our products may have a material adverse effect on our business, results of operations and financial condition.

If we cannot meet requirements under our license agreements, we could lose the rights to our products, which could have a material adverse effect on our business.

We depend on licensing agreements with third parties to maintain the intellectual property rights to certain of our product candidates. Our license agreements require us to make payments and satisfy performance obligations in order to maintain our rights under these agreements. All of these agreements last either throughout the life of the patents that are the subject of the agreements, or with respect to other licensed technology, for a number of years after the first commercial sale of the relevant product.

In addition, we are responsible for the cost of filing and prosecuting certain patent applications and maintaining certain issued patents licensed to us. If we do not meet our obligations under our license agreements in a timely manner, we could lose the rights to our proprietary technology which could have a material adverse effect on our business, results of operations and financial condition.

Risks Relating to Our Operations in Israel

Potential political, economic and military instability in the State of Israel, where the majority of our senior management and our research and development facilities are located, may adversely affect our results of operations.

Our executive office and operations are located in the State of Israel. Accordingly, political, economic and military conditions in Israel directly affect our business. Since the State of Israel was established in 1948, a number of armed conflicts have occurred between Israel and its Arab neighbors. Any hostilities involving Israel or the interruption or

curtailment of trade between Israel and its present trading partners, or a significant downturn in the economic or financial condition of Israel, could affect adversely our operations and product development. Although Israel has entered into various agreements with Egypt, Jordan and the Palestinian Authority, there have been times since October 2000 when Israel has experienced an increase in unrest and terrorist activity. The establishment in 2006 of a government in the Gaza Strip by representatives of the Hamas militant group has created additional unrest and uncertainty in the region. Starting in December 2008, for approximately three weeks, Israel engaged in an armed conflict with Hamas in the Gaza Strip. Armed conflicts have taken place between Israel and Hamas in the Gaza Strip in 2008, 2012 and 2014. Our facilities in northern Israel are in range of rockets that were fired from Lebanon into Israel during a 2006 war with the Hizbollah in Lebanon, and suffered minimal damages during one of the rocket attacks. Our insurance policies do not cover us for the damages incurred in connection with these conflicts or for any resulting disruption in our operations. The Israeli government, as a matter of law, provides coverage for the reinstatement value of direct damages that are caused by terrorist attacks or acts of war; however, the government may cease providing such coverage or the coverage might not be enough to cover potential damages. If our facilities are damaged as a result of hostile action, our operations may be materially adversely affected.

In addition to the foregoing, since the end of 2010, numerous acts of protest and civil unrest have taken place in several countries in the Middle East and North Africa, many of which involved significant violence. Civil unrest in Egypt, which borders Israel, has resulted in significant changes to the country’s government. There is currently a civil war in Syria, also bordering Israel, and Israel has been hit by rockets and mortars originating from Syria. The ultimate effect of these developments on the political and security situation in the Middle East and on Israel’s position within the region is not clear at this time.

Our operations may be disrupted by the obligations of our personnel to perform military service which could have a material adverse effect on our business.

Many of our male employees in Israel, including members of senior management, are obligated to perform up to one month (in some cases more) of annual military reserve duty until they reach the age of 45 and, in the event of a military conflict, could be called to active duty. Our operations could be disrupted by the absence of a significant number of our employees related to military service or the absence for extended periods of military service of one or more of our key employees. A disruption could have a material adverse effect on our business.

Because a certain portion of our expenses is incurred in New Israeli Shekels, our results of operations may be seriously harmed by currency fluctuations and inflation.

We report our financial statements in U.S. dollars, our functional currency. Although most of our expenses are incurred in U.S. dollars, we pay a portion of our expenses in New Israeli Shekels, or NIS, and as a result, we are exposed to risk to the extent that the inflation rate in Israel exceeds the rate of devaluation of the NIS in relation to the U.S. dollar or if the timing of these devaluations lags behind inflation in Israel. In that event, the U.S. dollar cost of our operations in Israel will increase and our U.S. dollar-measured results of operations will be adversely affected. To the extent that the value of the NIS increases against the dollar, our expenses on a dollar cost basis increase. Our operations also could be adversely affected if we are unable to guard against currency fluctuations in the future. To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rate of the U.S. dollar against the NIS. These measures, however, may not adequately protect us from material adverse effects.

The tax benefits available to us require that we meet several conditions and may be terminated or reduced in the future, which would increase our taxes.

We are able to take advantage of tax exemptions and reductions resulting from the “Approved Enterprise” status of our facilities in Israel. To remain eligible for these tax benefits, we must continue to meet certain conditions, including making specified investments in property and equipment, and financing at least 30% of such investments with share capital. If we fail to meet these conditions in the future, the tax benefits would be canceled and we may be required to refund any tax benefits we already have enjoyed. These tax benefits are subject to investment policy by the Investment Center and may not be continued in the future at their current levels or at any level. In recent years the Israeli government has reduced the benefits available and has indicated that it may further reduce or eliminate some of these benefits in the future. The termination or reduction of these tax benefits or our inability to qualify for additional “Approved Enterprise” approvals may increase our tax expenses in the future, which would reduce our expected profits and adversely affect our business and results of operations. Additionally, if we increase our activities outside of Israel, for example, by future acquisitions, such increased activities generally may not be eligible for inclusion in Israeli tax

benefit programs.

The Israeli government grants we have received for certain research and development expenditures restrict our ability to manufacture products and transfer technologies outside of Israel and require us to satisfy specified conditions. If we fail to satisfy these conditions, we may be required to refund grants previously received together with interest and penalties which could have a material adverse effect on our business and results of operations.

Our research and development efforts have been financed, in part, through grants that we have received from NATI. We, therefore, must comply with the requirements of the Research Law. Under the Research Law we are prohibited from manufacturing products developed using these grants outside of the State of Israel without special approvals, although the Research Law does enable companies to seek prior approval for conducting manufacturing activities outside of Israel without being subject to increased royalties. We may not receive the required approvals for any proposed transfer of manufacturing activities. Even if we do receive approval to manufacture products developed with government grants outside of Israel, we may be required to pay an increased total amount of royalties (possibly up to 300% of the grant amounts plus interest), depending on the manufacturing volume that is performed outside of Israel, as well as at a possibly increased royalty rate. This restriction may impair our ability to outsource manufacturing or engage in similar arrangements for those products or technologies.

Additionally, under the Research Law, Protalix Ltd. is prohibited from transferring NATI-financed technologies and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the approval of NATI Council or the Research Committee. Protalix Ltd. may not receive the required approvals for any proposed transfer and, if received, Protalix Ltd. may be required to pay NATI a portion of the consideration that it receives upon any sale of such technology by a non-Israeli entity. The scope of the support received, the royalties that Protalix Ltd. has already paid to NATI, the amount of time that has elapsed between the date on which the know-how was transferred and the date on which NATI grants were received and the sale price and the form of transaction will be taken into account in order to calculate the amount of the payment to NATI. Approval of the transfer of technology to residents of the State of Israel is required, and may be granted in specific circumstances only if the recipient abides by the provisions of applicable laws, including the restrictions on the transfer of know-how and the obligation to pay royalties. No assurance can be made that approval to any such transfer, if requested, will be granted.

These restrictions may impair our ability to sell our technology assets or to outsource manufacturing outside of Israel. The restrictions will continue to apply for a certain period of time even after we have repaid the full amount of royalties payable for the grants. For the years ended December 31, 2015, 2016 and 2017, we recorded grants totaling $4.9 million, $5.8 million and $3.3 million from NATI, respectively. The grants represent 19.5%, 19.1% and 10.4%, respectively, of our gross research and development expenditures for the years ended December 31, 2015, 2016 and 2017. If we fail to satisfy the conditions of the Research Law, we may be required to refund certain grants previously received together with interest and penalties, and may become subject to criminal charges, any of which could have a material adverse effect on our business, results of operations and financial condition.

Investors may have difficulties enforcing a U.S. judgment, including judgments based upon the civil liability provisions of the U.S. federal securities laws against us, our executive officers and most of our directors or asserting U.S. securities laws claims in Israel.

All of our directors and executive officers are residents of Israel, and accordingly, most of their assets and our assets are located outside the United States. Service of process upon our non-U.S. resident directors and officers and enforcement of judgments obtained in the United States against us, some of our directors and executive officers may be difficult to obtain within the United States. We have been informed by our legal counsel in Israel that investors may find it difficult to assert claims under U.S. securities laws in original actions instituted in Israel or obtain a judgment based on the civil liability provisions of U.S. federal securities laws against us, our officers and our directors. Israeli courts may refuse to hear a claim based on a violation of U.S. securities laws against us or our officers and directors because Israel is not the most appropriate forum to bring such a claim. In addition, even if an Israeli court agrees to hear a claim, it may determine that Israeli law and not U.S. law is applicable to the claim. If U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact which can be a time-consuming and costly process. Certain matters of procedure will also be governed by Israeli law. There is little binding case law in Israel addressing the matters described above.

Israeli courts might not enforce judgments rendered outside Israel which may make it difficult to collect on judgments rendered against us. Subject to certain time limitations, an Israeli court may declare a foreign civil judgment enforceable only if it finds that:

- the judgment was rendered by a court which was, according to the laws of the state of the court, competent to render the judgment;
- the judgment may no longer be appealed;
- the obligation imposed by the judgment is enforceable according to the rules relating to the enforceability of judgments in Israel and the substance of the judgment is not contrary to public policy; and
- the judgment is executory in the state in which it was given.

Even if these conditions are satisfied, an Israeli court will not enforce a foreign judgment if it was given in a state whose laws do not provide for the enforcement of judgments of Israeli courts (subject to exceptional cases) or if its enforcement is likely to prejudice the sovereignty or security of the State of Israel. An Israeli court also will not declare a foreign judgment enforceable if:

- the judgment was obtained by fraud;
- there is a finding of lack of due process;
- the judgment was rendered by a court not competent to render it according to the laws of private international law in Israel;
- the judgment is at variance with another judgment that was given in the same matter between the same parties and that is still valid; or
- at the time the action was brought in the foreign court, a suit in the same matter and between the same parties was pending before a court or tribunal in Israel.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our manufacturing facility and executive offices are located in Carmiel, Israel. The facilities currently contain approximately 20,000 sq/ft of manufacturing space and additional 48,000 sq/ft of laboratory, warehouse and office space and are leased at a rate of approximately $65,000 per month. In addition, we are entitled to use an additional 13,000 sq/ft in the same facility, which we intend to utilize in connection with an anticipated expansion of our manufacturing facilities. Our facilities are equipped with the requisite laboratory services required to conduct our business, and we believe that the existing facilities are adequate to meet our needs for the foreseeable future. Our original lease for the facility was in effect until 2016, at which time we extended the term until 2021. We retain two addition options to extend the term for a five-year period, for an aggregate of 10 additional years. Upon the exercise of each remaining option to extend the term of the lease, if any, the then current base rent shall be increased by 10%.

Item 3. Legal Proceedings

We are not involved in any material legal proceedings.

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

Our common stock is traded on the NYSE American under the symbol "PLX." Our common stock is also listed on the TASE under the symbol "PLX." The following table sets forth the quarterly high and low closing prices for our common stock on the NYSE American.

	Price Range	
	High	Low
Fourth Quarter 2017	$0.83	$0.57
Third Quarter 2017	$0.84	$0.49
Second Quarter 2017	$1.34	$0.78
First Quarter 2017	$1.44	$0.41
Fourth Quarter 2016	$0.57	$0.29
Third Quarter 2016	$0.67	$0.56
Second Quarter 2016	$0.90	$0.64
First Quarter 2016	$1.02	$0.76

These quotations reflect prices between dealers and do not include retained mark-ups, mark-downs and commissions and may not necessarily represent actual transactions. There were approximately 80 holders of record of our common stock at March 1, 2018. A substantially greater number of holders of our common stock are "street name" or beneficial holders, whose shares are held of record by banks, brokers and other financial institutions. To date, we have not declared or paid any cash dividends on our common stock. We do not anticipate paying any dividends on our common stock in the foreseeable future.

STOCK PERFORMANCE GRAPH

The following graph compares the cumulative total shareholder return data for our common stock from December 31, 2012 through December 31, 2017 to the cumulative return over such time period of (i) The NYSE American Index and (ii) The Nasdaq Biotechnology Index. The graph assumes an investment of $100 on December 31, 2012 in each of our common stock, the stocks comprising the NYSE American Index and the stocks comprising the Nasdaq Biotechnology Index, including dividend reinvestment, if any.

The stock price performance shown on the graph below represents historical price performance and is not necessarily indicative of any future stock price performance. Notwithstanding anything to the contrary set forth in any of our previous filings under the Securities Act or the Exchange Act, which might incorporate future filings made by us under those statutes, this Stock Performance Graph will not be incorporated by reference into any of those prior filings, nor will such report or graph be incorporated by reference into any future filings made by us under those Acts.

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Item 6. Selected Financial Data

The selected consolidated financial data below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. The selected consolidated statements of operations data for the years ended December 31, 2017, 2016 and 2015 and the selected consolidated balance sheet data as of December 31, 2017 and 2016, are derived from the audited consolidated financial statements included elsewhere in this Annual Report. The statement of operations data for the years ended December 31, 2014 and 2013 and the balance sheet data as of December 31, 2015, 2014 and 2013 are derived from audited financial statements not included in this Annual Report. We adopted, retrospectively, ASU 2014-08 during 2015 regarding discontinued operations which resulted in the reclassification of prior year amounts. The historical results presented below are not necessarily indicative of future results.

	Year Ended December 31,				
	2013	2014	2015	2016	2017
	(in thousands, except share and per share amounts)				
Consolidated Statement of Operations Data:					
Revenues	$-	$3,523	$4,364	$9,199	$19,242
Cost of revenues	-	630	730	8,398	15,231
Gross profit	-	2,893	3,634	801	4,011
Research and development expenses, net	26,012	22,224	20,025	24,608	28,834
Selling, general and administrative expenses	8,051	9,228	7,279	9,356	11,530
Financial income (expenses), net	(674)	(4,739)	(3,612)	3,987	(48,923)
Loss from continuing operations	$34,737	$33,298	$27,282	$29,176	$(85,276)
(Loss) income from discontinued operations	6,947	3,355	85,319	(189)	
Net income (loss) for the year	(27,790)	(29,943)	58,037	(29,365)	(85,276)
Net income (loss) per share of common stock, basic and diluted:					
Loss from continuing operations	$(0.38)	$(0.36)	$(0.29)	$(0.29)	$(0.65)
(Loss) income from discontinued operations	0.08	0.04	0.90	(0.00)	
Net (loss) income per share of common stock	(0.30)	(0.32)	0.61	(0.29)	(0.65)
Weighted average number of shares of common stock used in computing net loss per share of common stock	92,368,138	92,891,846	94,922,390	101,387,704	131,085,958
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$86,398	$54,767	$76,374	$63,281	$51,163
All other assets	26,935	23,590	20,879	18,966	21,051
Total assets	113,192	78,357	97,253	82,247	72,214
Current liabilities	26,696	64,354	11,235	66,212	22,752

Long term convertible notes	67,048	67,351	67,796	19,343	46,267
Total liabilities	140,138	133,958	86,380	92,204	103,507
Total stockholders' equity (capital deficiency)	(26,946)	(55,601)	10,873	(9,957)	(31,293)

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis, particularly with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read "Risk Factors" in Item 1A of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins based on our proprietary ProCellEx® protein expression system. We developed our first commercial drug product, Elelyso®, using our ProCellEx system and we are now focused on utilizing the system to develop a pipeline of proprietary, clinically superior versions of recombinant therapeutic proteins that primarily target large, established pharmaceutical markets and that in most cases rely upon known biological mechanisms of action. With our experience to date, we believe ProCellEx will enable us to develop additional proprietary recombinant proteins that are therapeutically superior to existing recombinant proteins currently marketed for the same indications including applying the unique properties of our ProCellEx system for the oral delivery of therapeutic proteins.

On October 19, 2017, Protalix Ltd., our wholly-owned subsidiary, and Chiesi entered into the Chiesi Agreement pursuant to which Chiesi was granted an exclusive, license for all markets outside of the United States to commercialize pegunigalsidase alfa. Pegunigalsidase alfa is our chemically modified version of the recombinant protein alpha-Galactosidase-A protein that is currently being evaluated in phase III clinical trials for the treatment of Fabry disease. Under the terms and conditions of the Chiesi Agreement, Protalix Ltd. retained the right to commercialize pegunigalsidase alfa in the United States. Under the Chiesi Agreement, Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to $25 million in development costs, capped at $10 million per year. Protalix Ltd. is also eligible to receive an additional up to $320 million, in the aggregate, in regulatory and commercial milestone payments. Protalix Ltd. agreed to manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi is required to make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa. The Chiesi Agreement also provides for reimbursement by Chiesi of certain costs to be incurred by Protalix Ltd.

In December 2017, the European Commission granted Orphan Drug Designation for pegunigalsidase alfa for the treatment of Fabry disease. The designation was granted after the COMP issued a positive opinion supporting the

designation noting that we had established that there was medically plausible evidence that pegunigalsidase alfa will provide a significant benefit over existing approved therapies in the European Union for the treatment of Fabry disease. The COMP cited clinical and non-clinical justifications we provided to establish the significant benefit of pegunigalsidase alfa, noting that the COMP considered the justifications to constitute a clinically relevant advantage. Orphan Drug Designation for pegunigalsidase alfa qualifies Protalix Ltd. for access to a centralized marketing authorization procedure, including applications for inspections and for protocol assistance. If the orphan drug designation is maintained at the time pegunigalsidase alfa is approved for marketing in the European Union, if at all, we expect that PRX-102 will benefit from 10 years of market exclusivity within the European Union. The market exclusivity will not have any effect on Fabry disease treatments already approved at that time.

In January 2018, the FDA granted Fast Track designation to PRX-102. Fast Track designation is a process designed to facilitate the development and expedite the review of drugs and vaccines for serious conditions that fill an unmet medical need.

On May 1, 2012, the FDA approved for sale our first commercial product, taliglucerase alfa for injection, an ERT for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease. Subsequently, taliglucerase alfa was approved for marketing by the regulatory authorities of other countries. Taliglucerase alfa is called alfataliglicerase in Brazil and certain other Latin American countries, where it is marketed under the name alfataliglicerase. Taliglucerase alfa is marketed under the name Elelyso in other territories.

Since its approval by the FDA, taliglucerase alfa has been marketed by Pfizer, as provided in the Pfizer Agreement. In October 2015, we entered into the Amended Pfizer Agreement which amends and restates the Pfizer Agreement in its entirety. Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso in exchange for a cash payment equal to $36.0 million. As part of the sale, we agreed to transfer our rights to Elelyso in Israel to Pfizer, while gaining full rights to Elelyso in Brazil. We will continue to manufacture drug substance for Pfizer, subject to certain terms and conditions. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all revenues globally for Elelyso, excluding Brazil, where we are responsible for all expenses and retain all revenues.

For the first 10-year period after the execution of the Amended Pfizer Agreement, we have agreed to sell drug substance to Pfizer for the production of Elelyso, and Pfizer maintains the right to extend the supply period for up to two additional 30-month periods subject to certain terms and conditions. Any failure to comply with our supply commitments may subject us to substantial financial penalties, which will have a material adverse effect on our business, results of operations and financial condition. The Amended Pfizer Agreement also includes customary provisions regarding cooperation for regulatory matters, patent enforcement, termination, indemnification and insurance requirements.

On June 18, 2013, we entered into the Brazil Agreement with Fiocruz, an arm of the Brazilian MoH, for taliglucerase alfa.

In 2017, we received a purchase order from the Brazilian MoH for the purchase of approximately $24.3 million of alfataliglicerase for the treatment of Gaucher patients in Brazil. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. Fiocruz’s purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in the best interest of our company.

We are developing an innovative product pipeline using our ProCellEx protein expression system. Our product pipeline currently includes, among other candidates:

(1) pegunigalsidase alfa, or PRX-102, a therapeutic protein candidate for the treatment of Fabry disease, a rare, genetic lysosomal disorder in humans, currently in an ongoing phase III clinical trial.

(2) alidornase alfa, or PRX-110, a proprietary plant cell recombinant human Deoxyribonuclease 1 under development for the treatment of CF, to be administered by inhalation. We recently completed a phase IIa efficacy and safety study of alidornase alfa for the treatment of CF.

(3) OPRX-106, our oral antiTNF product candidate which is being developed as an orally-delivered anti-inflammatory treatment using plant cells as a natural capsule for the expressed protein. We expect to release final data generated in our phase II clinical trial of OPRX-106 for the treatment of ulcerative colitis by the end of March, 2018.

Except for the rights to commercialize taliglucerase alfa worldwide (other than Brazil), which we licensed to Pfizer, and the rights to pegunigalsidase alfa Chiesi outside the United States, which we licensed to Chiesi, we hold the worldwide commercialization rights to all of our proprietary development candidates. In addition, we continuously evaluate potential strategic marketing partnerships as well as collaboration programs with biotechnology and pharmaceutical companies and academic research institutes.

Critical Accounting Policies

Our significant accounting policies are more fully described in Note 1 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K. We believe that the accounting policies below are critical for one to fully understand and evaluate our financial condition and results of operations.

The discussion and analysis of our financial condition and results of operations is based on our financial statements, which we prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate such estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Functional Currency

The currency of the primary economic environment in which our operations are conducted is the U.S. dollar. All of our revenues are derived in dollars. In addition, most of our expenses and capital expenditures are incurred in dollars, and the major source of our financing has been provided in dollars.

Revenues

Our primary sources of revenues include our sales of taliglucerase alfa in Brazil and of drug substance to Pfizer under our Amended Pfizer Agreement. We recognize revenue when the earnings process is complete, which is when revenue is realized or realizable and earned, there is persuasive evidence a revenue arrangement exists, delivery of goods or services has occurred, the sales price is fixed or determinable and collectability is reasonably assured.

We also generate revenues from the Chiesi Agreement. As Chiesi is obligated to acquire pegunigalsidase alfa from us, and has limited, immaterial rights until then, the development services performed under the agreement are not considered to have a stand-alone value, and will be viewed as one unit of account - manufacturing and supply of the drug. Therefore payments received from Chiesi prior to the fulfillment of the one unit of account will be deferred until the commencement of the commercial manufacturing. We will recognize revenues after the commencement of drug supply over the period of the product’s sales according to our best estimate of sale price.

Discontinued Operations

Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso. As part of the sale, we agreed to transfer our rights to Elelyso in Israel to Pfizer while gaining full rights to Elelyso in Brazil. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all of the revenues, globally, for Elelyso, excluding Brazil where we are responsible for all expenses and retain all revenues. The Amended Pfizer Agreement eliminated Pfizer's entitlement to annual payments of up to $12.5 million in relation to commercialization of Elelyso in Brazil. For further details please see notes 2 and 12 to the financial statements.

We accounted for the sale of our share in the collaboration created under the initial Pfizer Agreement, including the transfer of our rights to Elelyso in Israel, in accordance with ASU No. 2014-08.

Certain of our assets and liabilities associated with our share in the former collaboration, including our rights to Elelyso in Israel, have been segregated and classified as assets and liabilities of discontinued operations, as appropriate, in our consolidated balance sheets as of December 31, 2016 and 2017. In addition, certain financial information related to our share in the former collaboration, including our rights to Elelyso in Israel, have been segregated from continuing operations and have been reported as discontinued operations in our consolidated statements of operations. See note 12 to the financial statements.

Research and Development Expense

We expect our research and development expense to remain our primary expense in the near future as we continue to develop our product candidates. Research and development expense consists of:

- internal costs associated with research and development activities;
- payments made to third party contract research organizations, investigative/clinical sites and consultants;

- manufacturing development costs;
- personnel-related expenses, including salaries, benefits, travel, and related costs for the personnel involved in research and development;
- activities relating to the advancement of product candidates through preclinical studies and clinical trials; and
- facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, as well as laboratory and other supplies.

The following table identifies our current major research and development projects:

Project	**Status**	**Expected Near Term Milestones**
PRX-102 – pegunigalsidase alfa	Phase III clinical trial, ongoing	Completion of enrollment in trial and interim data analysis
PRX-110 – alidornase alfa	Phase IIa completed	Design of next clinical trial
OPRX-106 – Oral antiTNF	Phase IIa completed	Full results for the study

We anticipate incurring increasing costs in connection with the continued development of all of the product candidates in our pipeline. Our internal resources, employees and infrastructure are not tied to any individual research project and are typically deployed across all of our projects. We currently do not record and maintain research and development costs per project.

The costs and expenses of our projects are partially funded by grants we have received from NATI. Each grant is deducted from the related research and development expenses as the costs are incurred. For additional information regarding the grant process, see “Business—Israeli Government Programs— Encouragement of Industrial Research, Development and Technology Innovation, 1984” in Item 1 of this Annual Report. There can be no assurance that we will continue to receive grants from NATI in amounts sufficient for our operations, if at all. In addition, under the Chiesi Agreement, Protalix Ltd. is entitled to payments of up to $25 million to cover development costs for pegunigalsidase alfa, capped at $10 million per year.

At this time, due to the inherently unpredictable nature of preclinical and clinical development processes and given the early stage of our preclinical product development programs, we are unable to estimate with any certainty the costs we will incur in the continued development of the product candidates in our pipeline for potential commercialization. Clinical development timelines, the probability of success and development costs can differ materially from expectations. The current focus of our product development efforts are on pegunigalsidase alfa. Our future research and development expenses for pegunigalsidase alfa and the other product candidates will depend on the clinical success of each product candidate, as well as ongoing assessments of each product candidate’s commercial potential. In addition, we cannot forecast with any degree of certainty which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect

our development plans and capital requirements. See “Risk Factors—If we are unable to develop and commercialize our product candidates, our business will be adversely affected” and “—We may not obtain the necessary U.S., EMA or other worldwide regulatory approvals to commercialize our drug candidates in a timely manner, if at all, which would have a material adverse effect on our business, results of operations and financial condition.”

We expect our research and development expenses to continue to be our primary expense in the future as we continue the advancement of our clinical trials and preclinical product development programs for our product candidates, particularly with respect to the development of pegunigalsidase alfa. The lengthy process of completing clinical trials and seeking regulatory approvals for our product candidates requires expenditure of substantial resources. Any failure or delay in completing clinical trials, or in obtaining regulatory approvals, could cause a delay in generating product revenue and cause our research and development expense to increase and, in turn, have a material adverse effect on our operations. Due to the factors set forth above, we are not able to estimate with any certainty when we would recognize any net cash inflows from our projects. See “Risk Factors—Clinical trials are very expensive, time-consuming and difficult to design and implement and may result in unforeseen costs which may have a material adverse effect on our business, results of operations and financial condition.”

Share-Based Compensation

The discussion below regarding share-based compensation relates to our share-based compensation.

In accordance with the guidance, we record the benefit of any grant to a non-employee and remeasure the benefit in any future vesting period for the unvested portion of the grants, as applicable. In addition, we use the straight-line accounting method for recording the benefit of the entire grant, unlike the graded method we use to record grants made to employees.

We measure share-based compensation cost for all share-based awards at the fair value on the grant date and recognition of share-based compensation over the service period for awards that we expect will vest. The fair value of stock options is determined based on the number of shares granted and the price of our ordinary shares, and calculated based on the Black-Scholes valuation model. We recognize such value as expense over the service period, net of estimated forfeitures, using the accelerated method.

The guidance requires companies to estimate the expected term of the option rather than simply using the contractual term of an option. Because of lack of data on past option exercises by employees, the expected term of the options could not be based on historic exercise patterns. Accordingly, we adopted the simplified method, according to which companies may calculate the expected term as the average between the vesting date and the expiration date, assuming the option was granted as a “plain vanilla” option.

In performing the valuation, we assumed an expected 0% dividend yield in the previous years and in the next years. We do not have a dividend policy and given the lack of profitability, dividends are not expected in the foreseeable future, if at all. The guidance stipulates a number of factors that should be considered when estimating the expected volatility, including the implied volatility of traded options, historical volatility and the period that the shares of the company are being publicly traded.

The risk-free interest rate used in the valuation of the options is based on the implied yield of U.S. federal reserve zero–coupon government bonds. The remaining term of the bonds used for each valuation was equal to the expected term of the grant. This methodology has been applied to all grants valued by us. The guidance requires the use of a risk–free interest rate based on the implied yield currently available on zero–coupon government issues of the country in whose currency the exercise price is expressed, with a remaining term equal to the expected life of the option being valued. This requirement has been applied for all grants valued as part of this report.

Convertible Notes

All outstanding convertible notes are accounted for using the guidance set forth in the Financial Accounting Standards Board, or FASB, Accounting Standards Codification (ASC) 815 requiring that we determine whether the embedded conversion option must be separated and accounted for separately. ASC 470-20 regarding debt with conversion and other options requires the issuer of a convertible debt instrument that may be settled in cash upon conversion to separately account for the liability (debt) and equity (conversion option) components of the instrument in a manner that reflects the issuer's nonconvertible debt borrowing rate. We account for the 4.5% convertible notes as liability, on an aggregated basis, in their entirety. The conversion feature for our 7.5% convertible notes is accounted for as a derivative which is bifurcated from the debt host contract and is measured at fair value through the statement of operations.

Issuance costs regarding the issuance of our 7.5% convertible notes were allocated to the liability, equity component, derivative and shares of common stock based on their relative fair values. Issuance costs that were allocated to liability will be amortized using the effective interest rate, other than issuance costs that were allocated to derivative, which were expensed immediately.

The debt discount and debt issuance costs regarding the issuance of 4.5% convertible notes are deferred and amortized over the applicable convertible period (5 years).

Year Ended December 31, 2017 Compared to the Year Ended December 31, 2016

Revenues

We recorded revenues of $19.2 million for the year ended December 31, 2017, an increase of approximately $10.0 million, or 109%, compared to revenues of $9.2 million for the year ended December 31, 2016. Revenues include $7.1 million of products sold in Brazil and $12.1 million of drug substance sold to Pfizer The increase resulted from an increase in the amount of $3.1 million of product sold to Brazil and $7.0 million of drug substance sold to Pfizer.

Cost of Revenues

Cost of revenues was $15.2 million for the year ended December 31, 2017, an increase of $6.8 million or 81%, compared to the cost of revenues of $8.4 million for the year ended December 31, 2016. The increase resulted primarily from costs related to the production of drug substance for sale to Pfizer, and of drug product for sale to Brazil.

Research and Development Expenses

Research and development expenses were $32.2 million for the year ended December 31, 2017, an increase of $1.8 million, or 6% from $30.4 million for the year ended December 31, 2016. The increase resulted primarily from an increase of $2.4 million in clinical trial related costs, which was partially offset by a decrease of $0.7 million in materials.

We expect research and development expenses to continue to be our primary expense as we enter into a more advanced stage of preclinical and clinical trials for certain of our product candidates, primarily with respect to pegunigalsidase alfa.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $11.5 million for the year ended December 31, 2017, an increase of $2.2 million, or 23%, from $9.4 million for the year ended December 31, 2016. The increase resulted primarily from an increase in sales and marketing activities in connection with the sale of alfataliglicerase in Brazil.

Financial Expenses and Income

Financial expense was $48.9 million for the year ended December 31, 2017, compared to financial income of $4.0 million for the year ended December 31, 2016. Financial expenses included a charge of $38.1 million as a result of the re-measurement of the fair value of the 7.5% convertible notes embedded derivative. In addition, financial expenses is comprised primarily from interest expense on convertible notes.

Year Ended December 31, 2016 Compared to the Year Ended December 31, 2015

Revenues

We recorded revenues of $9.2 million for the year ended December 31, 2016, an increase of approximately $4.8 million, or 111%, compared to revenues of $4.4 million for the year ended December 31, 2015. Revenues represent products sold in Brazil and drug substance sold to Pfizer. The increase is mainly due to an increase of $4.8 million of drug substance sold to Pfizer.

Cost of Revenues

Cost of revenues was $8.4 million for the year ended December 31, 2016 compared to the cost of revenues of $730,000 for the year ended December 31, 2015. The increase is mainly due to cost of revenues that were attributed to an increase in the amount of drug substance sold to Pfizer at cost during the period and that a substantial portion of activities performed during 2015 were attributed to the development and production of PRX-102 for the entire period during which the phase III clinical trial is to be performed.

Research and Development Expenses

Research and development expenses were $30.4 million for the year ended December 31, 2016, an increase of $5.5 million, or 22% from $24.9 million for the year ended December 31, 2015. The increase resulted primarily from an increase of $3.7 million in clinical trial related costs.

We expect research and development expenses to continue to be our primary expense as we enter into a more advanced stage of preclinical and clinical trials for certain of our product candidates.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $9.4 million for the year ended December 31, 2016, an increase of $2.1 million, or 29%, from $7.3 million for the year ended December 31, 2015. The increase resulted primarily from an increase in sales and marketing activities in connection with the sale of alfataliglicerase in Brazil.

Financial Expenses and Income

Financial income was $4.0 million for the year ended December 31, 2016, compared to financial expense of $3.6 million for the year ended December 31, 2015. Financial income for the year ended December 31, 2016 resulted primarily from the exchange of $54.1 million of our 4.5% notes into $40.2 million aggregate principal amount of 7.5% senior secured notes and 23.8 million shares of our common stock. The exchange was accounted for as extinguishment of notes, and the difference between the net carrying value of the 4.5% notes exchanged and the fair value of the new notes and shares issued were accounted for as a gain on extinguishment of $14.1 million. The financial income was partially offset by $3.2 million of expenses resulting primarily from interest expense related to our outstanding convertible notes and by $6.5 million of change in fair value of convertible notes embedded derivative.

Liquidity and Capital Resources

Sources of Liquidity

As a result of our significant research and development expenditures and the lack of significant revenue from sales of taliglucerase alfa, we have generated operating losses from our continuing operations since our inception. To date, we have funded our operations primarily with proceeds equal to $31.3 million from the sale of shares of convertible preferred and ordinary shares of Protalix Ltd., and an additional $14.1 million in connection with the exercise of warrants issued in connection with the sale of such shares, through December 31, 2008. In addition, on October 25, 2007, we generated gross proceeds of $50 million in connection with an underwritten public offering of our common stock and on each of March 23, 2011 and February 22, 2012, we generated gross proceeds of $22.0 million and $27.2 million, respectively, in connection with underwritten public offerings of our common stock. We believe that the funds currently available to us as are sufficient to satisfy our capital needs for at least 12 months.

The following table summarizes our public funding sources since 2007:

Security	**Year**	**Number of Shares**	**Amount**
Common Stock	2007	10,000,000	$50,000,000
Common Stock	2011	4,000,000	$22,000,000
Common Stock	2012	5,175,000	$27,168,750

In addition to the foregoing, on September 18, 2013, we completed a private placement of $69.0 million in aggregate principal amount of 4.50% convertible notes due 2018, including $9.0 million aggregate principal amount of Notes related to the offering's initial purchaser's over-allotment option, which was exercised in full. In December 2016, we completed a private placement of $22.5 million in aggregate principal amount of 7.5% convertible notes due 2021. Finally, on July 25, 2017, we completed a private placement of an additional $10.0 million in aggregate principal amount of 7.5% convertible notes due 2021.

Pfizer paid Protalix Ltd. $60.0 million as an upfront payment in connection with the execution of the Pfizer Agreement and subsequently paid to Protalix Ltd. an additional $5.0 million upon Protalix Ltd.'s meeting a certain milestone. Protalix Ltd. also received a milestone payment of $25.0 million in connection with the FDA's approval of taliglucerase alfa in May 2012. Pfizer has also paid Protalix Ltd. $8.3 million in connection with the successful achievement of certain milestones under a clinical development agreement between Pfizer and Protalix Ltd. In connection with the execution of the Amended Pfizer Agreement, we received a $36.0 million payment from Pfizer, and Pfizer purchased 5,649,079 shares of our common stock for $10.0 million.

In the fourth quarter of 2017, Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the Chiesi Agreement.

Cash Flows

Net cash used in operations was $10.0 million for the year ended December 31, 2017. The net loss from continuing operations for the year ended December 31, 2017 of $85.3 million was partially offset by a change of $38.1 million in the fair value of convertible notes embedded derivative and an increase of $26 million in deferred revenues. Net cash used in investing activities for the year ended December 31, 2017 was $1.1 million and consisted primarily of purchase of property and equipment. Net cash used in financing activities was $1.4 million which consisted of cash settlement of $11.0 million for certain conversions of our convertible notes which was partially offset by $9.5 million of net proceeds from the issuance of our 7.5% convertible notes.

Net cash used in operations was $32.1 million for the year ended December 31, 2016. The net loss from continuing operations for the year ended December 31, 2016 of $29.2 million was further increased by $7.6 million non cash financial income, but was partially offset by $2.0 million in depreciation and a $2.1 million increase in accounts payable. Net cash used in investing activities for the year ended December 31, 2016 was $967,000 and consisted primarily of equipment purchases. Net cash provided by financing activities was $19.7 million and consisted primarily of proceeds from the private offering of our 7.5% convertible notes.

Future Funding Requirements

We expect to continue to incur significant expenditures in the near future, including significant research and development expenses related primarily to the clinical trials of PRX-102. We believe that our existing cash and cash equivalents will be sufficient for at least 12 months. We have based this estimate on assumptions that are subject to change and may prove to be wrong, and we may be required to use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials.

Our future capital requirements will depend on many other factors, including our progress in commercializing alfataliglicerase in Brazil, the progress and results of our clinical trials, the duration and cost of discovery and preclinical development and laboratory testing and clinical trials for our product candidates, conversions of our convertible notes from time to time, the timing and outcome of regulatory review of our product candidates, the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights, the number and development requirements of other product candidates that we pursue and the costs of commercialization activities, including product marketing, sales and distribution.

We may need to finance our future cash needs through corporate collaboration, licensing or similar arrangements, public or private equity offerings or debt financings. We currently do not have any commitments for future external funding, except with respect to the development-related payments and milestone payments that may become payable under the Chiesi Agreement. We may need to raise additional funds more quickly if one or more of our assumptions prove to be incorrect or if we choose to expand our product development efforts more rapidly than we presently anticipate. We may also decide to raise additional funds even before we need them if the conditions for raising capital are favorable. Any sale of additional equity or debt securities will likely result in dilution to our shareholders. The incurrence of indebtedness would result in increased fixed obligations and could also result in covenants that would restrict our operations. Additional equity or debt financing, grants or corporate collaboration and licensing arrangements may not be available on acceptable terms, if at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our planned commercialization efforts or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently.

Effects of Inflation and Currency Fluctuations

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the years ended December 31, 2015, 2016 or 2017.

Currency fluctuations could affect us by increased or decreased costs mainly for goods and services acquired outside of Israel. We do not believe currency fluctuations have had a material effect on our results of operations during the years ended December 31, 2015, 2016 or 2017.

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements as of December 31, 2016 and 2017.

Recently Issued Accounting Pronouncements

Certain recently issued accounting pronouncements are discussed in Note 1(q) of the financial statements included in Item 8 of this Annual Report on Form 10-K.

Contractual Obligations

The following table summarizes our significant contractual obligations at December 31, 2017:

(U.S. dollars in thousands)	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Convertible notes	$83,004	$ 10,646	$8,860	$63,498	-
Operating lease obligations	$3,935	$ 1,349	$2,006	$580	-
Purchase obligations (1)	$3,668	$ 3,668	-	-	-
Certain clinical contract	$19,170	$ 8,614	$10,427	$129	-
Liability for employee rights upon retirement	$2,586	-	-	-	$ 2,586
Total	$112,363	$ 24,277	$21,293	$64,207	$ 2,586

(1) Represents open purchase orders issued to certain suppliers and other vendors mainly in connection with our research and development activities that were outstanding as of December 31, 2017.

The foregoing table does not include (i) annual license fees, which are immaterial, (ii) payments we may be required to make to certain of our licensors in the time periods set forth above upon the achievement of agreed-upon milestones

and (iii) royalty payments payable by us to certain of our licensors in connection with the commercial sale of our product candidates, if any. If all of the contingencies with respect to milestone payments under our research and license agreements are met, the aggregate milestone payments payable would be approximately $14.3 million and would be payable, if at all, as our projects progress over the course of a number of years. The royalty payments payable in connection with sales of each of our product candidates, if any, shall not exceed low, single-digit percentages of net sales of the product.

Selected Quarterly Financial Data (unaudited)

	Three Months Ended							
	2016				2017			
	(U.S. dollars in thousands)							
	March 31	June 30	Sept. 30	Dec. 31	March 31	June 30	Sept. 30	Dec. 31
Revenues	$679	$1,769	$4,670	2,081	$2,889	$6,358	$7,526	2,469
Gross profit	156	94	422	129	801	835	1,460	915
(Loss) income from continuing operations	(8,526)	(10,736)	(7,290)	(2,624)	(59,148)	450	(11,437)	(15,141)
Income (loss) from discontinued operations	(72)	(117)	0	0	-	-	-	
Net (loss) profit for the period	$(8,598)	$(10,853)	$(7,290)	$(2,624)	$(59,148)	$450	$(11,437)	$(15,141)
Earnings (loss) per share of common stock, basic and diluted:								
Loss from continuing operations	$(0.09)	$(0.11)	$(0.07)	$(0.02)	$(0.48)	$0.00	$(0.09)	$(0.11)
Income (loss) from discontinued operations	(0.00)	(0.00)	(0.00)	(0.00)				
Net basic income (loss) per share of common stock	$(0.09)	$(0.11)	$(0.07)	$(0.02)	$(0.48)	$0.00	$(0.09)	$(0.11)
Net diluted loss per share of common stock	$(0.09)	$(0.11)	$(0.07)	$(0.02)	$(0.48)	$(0.06)	$(0.09)	$(0.11)

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Currency Exchange Risk

The currency of the primary economic environment in which our operations are conducted is the dollar. Most of our revenues and approximately 50% of our expenses and capital expenditures are incurred in dollars, and a significant source of our financing has been provided in U.S. dollars. Since the dollar is the functional currency, monetary items maintained in currencies other than the dollar are remeasured using the rate of exchange in effect at the balance sheet dates and non-monetary items are remeasured at historical exchange rates. Revenue and expense items are remeasured at the average rate of exchange in effect during the period in which they occur. Foreign currency translation gains or losses are recognized in the statement of operations.

Approximately 35% of our costs, including salaries, expenses and office expenses, are incurred in NIS. Inflation in Israel may have the effect of increasing the U.S. dollar cost of our operations in Israel. If the U.S. dollar declines in value in relation to the NIS, it will become more expensive for us to fund our operations in Israel. A revaluation of 1% of the NIS will affect our loss before tax by less than 1%. The exchange rate of the U.S. dollar to the NIS, based on exchange rates published by the Bank of Israel, was as follows:

	Year Ended December 31,		
	2015	2016	2017
Average rate for period	3.887	3.841	3.600
Rate at year-end	3.902	3.845	3.467

To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rate of the U.S. dollar against the NIS. These measures, however, may not adequately protect us from material adverse effects due to the impact of inflation in Israel.

Interest Rate Risk

Our exposure to market risk is confined to our cash and cash equivalents. We consider all short term, highly liquid investments, which include short-term deposits with original maturities of three months or less from the date of purchase, that are not restricted as to withdrawal or use and are readily convertible to known amounts of cash, to be cash equivalents. The primary objective of our investment activities is to preserve principal while maximizing the interest income we receive from our investments, without increasing risk. We invest any cash balances primarily in

bank deposits and investment grade interest-bearing instruments. We are exposed to market risks resulting from changes in interest rates. We do not use derivative financial instruments to limit exposure to interest rate risk. Our interest gains may decline in the future as a result of changes in the financial markets.

Item 8. Financial Statements and Supplementary Data

See the Index to Consolidated Financial Statements on Page F-1 attached hereto.

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

We conducted an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this Form 10-K. The controls evaluation was conducted under the supervision and with the participation of management, including our Chief Executive Officer and Chief Financial Officer. Disclosure controls and procedures are controls and procedures designed to reasonably assure that information required to be disclosed in our reports filed under the Exchange Act, such as this Form 10-K, is recorded, processed, summarized and reported within the time periods specified in the Commission’s rules and forms. Disclosure controls and procedures are also designed to reasonably assure that such information is accumulated and communicated to our management, including the Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

The evaluation of our disclosure controls and procedures included a review of the controls' objectives and design, our implementation of the controls and their effect on the information generated for use in this Form 10-K. In the course of the controls evaluation, we reviewed identified data errors, control problems or acts of fraud, and sought to confirm that appropriate corrective actions, including process improvements, were being undertaken. This type of evaluation will be performed on a quarterly basis so that the conclusions of management, including the Chief Executive Officer and Chief Financial Officer, concerning the effectiveness of the disclosure controls and procedures can be reported in our periodic reports on Form 10-Q and Form 10-K. The overall goals of these various evaluation activities are to monitor our disclosure controls and procedures, and to modify them as necessary. Our intent is to maintain the disclosure controls and procedures as dynamic systems that change as conditions warrant.

Based on the controls evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the end of the period covered by this Form 10-K, our disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified by the Commission, and that material information related to our company and our consolidated subsidiaries are made known to management, including the Chief Executive Officer and Chief Financial Officer, particularly during the period when our periodic reports are being prepared.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles. Internal control over financial reporting includes those policies and procedures that: (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. generally accepted accounting principles, and that receipts and expenditures of our company are being made only in accordance with authorizations of management and our directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Management assessed our internal control over financial reporting as of December 31, 2017, the end of our fiscal year. Management based its assessment on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Management's assessment included evaluation of elements such as the design and operating effectiveness of key financial reporting controls, process documentation, accounting policies and our overall control environment.

Based on our assessment, management has concluded that our internal control over financial reporting was effective as of the end of the fiscal year to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles. We reviewed the results of management's assessment with the Audit Committee of our Board of Directors.

The effectiveness of our internal control over financial reporting as of December 31, 2017 has been audited by Kesselman & Kesselman, an independent registered public accounting firm, as stated in their report included herein.

Inherent Limitations on Effectiveness of Controls

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent or detect all error and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. The design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Further, because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, within a 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 simple error or mistake. Controls can also be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. The design of any system of controls is based in part on 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. Projections of any evaluation of controls effectiveness to future periods are subject to risks. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures.

Changes in internal controls

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15f and 15d-15f under the Exchange Act) that occurred during the year ended December 31, 2017 that have materially affected, or that are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information in our 2018 Proxy Statement regarding directors and executive officers appearing under the headings "Security Ownership of Certain Beneficial Owners and Management— Section 16(a) Beneficial Ownership Reporting Compliance" and "Proposal 1: Election of Directors" is incorporated by reference in this section.

Item 11. Executive Compensation

The information appearing in our 2018 Proxy Statement under the headings "Director Compensation," "Compensation Discussion and Analysis," "Report of the Compensation Committee," and "Executive Compensation" is incorporated by reference in this section.

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

The information appearing in our 2018 Proxy Statement under the heading "Security Ownership of Certain Beneficial Owners and Management" is incorporated by reference in this section.

Equity Compensation Plan Information

The following table provides information as of December 31, 2017 with respect to the shares of our common stock that may be issued under our existing equity compensation plan.

Plan Category	A Number of Securities to be Issued Upon Exercise of Outstanding Options	B Weighted Average Exercise Price of Outstanding Options	C Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column A)

Equity Compensation Plans Approved by Stockholders	4,929,617	3.59	2,554,075
Equity Compensation Plans Not Approved by Stockholders	-	-	-
Total	4,929,617	3.59	2,554,075

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

The information appearing in our 2018 Proxy Statement under the headings “Proposal 1: Election of Directors—Corporate Governance” and “—Certain Relationships and Related Transactions” is incorporated by reference in this section.

Item 14. Principal Accountant Fees and Services

The information appearing in our 2018 Proxy Statement under the heading “Proposal 4: Ratification of Appointment of Independent Registered Public Accounting Firm” is incorporated by reference in this section.

PART IV

Item 15. Exhibits and Financial Statement Schedules

The following documents are filed as part of this Annual Report on Form 10-K:

1. *Financial Statements*. The following Consolidated Financial Statements of Protalix BioTherapeutics, Inc. are included in Item 8 of this Annual Report on Form 10-K:

2. *Financial Statement Schedule.* Financial statement schedules have been omitted since they are either not required, are not applicable or the required information is shown in the consolidated financial statements or related notes.

3. *Exhibits.*

		Incorporated by Reference				
Exhibit Number	**Exhibit Description**	**Form**	**File Number**	**Exhibit**	**Date**	**Filed Herewith**
3.1	Certificate of Incorporation of the Company	8-K	333-48677	3.1	April 1, 2016	
3.2	Amendment to Certificate of Incorporation of the Company	Def 14A	001-33357	Appen. A	July 1, 2016	
3.3	Bylaws of the Company	8-K	001-33357	3.2	April 1, 2016	

4.1	Form of Restricted Stock Agreement/Notice	8-K	001-33357	4.1	July 18, 2012
4.2	Indenture, dated as of September 18, 2013, between Protalix BioTherapeutics, Inc. and The Bank of New York Mellon Trust Company, N.A., as Trustee	8-K	001-33357	4.1	September 18, 2013
4.3	Form of 4.50% Convertible Note due 2018	8-K	001-33357	4.2	September 18, 2013
4.4	Indenture, dated as of December 7, 2016, between Protalix BioTherapeutics, Inc. the guarantors party thereto, The Bank of New York Mellon Trust Company, N.A., as trustee and Wilmington Savings Fund Society, FSB, as collateral agent	8-K	001-33357	4.1	December 7, 2016

4.5	Form of 7.50% Convertible Note due 2018 (Issued in Financing)	8-K	001-33357	4.2	December 7, 2016
4.6	Form of 7.50% Convertible Note due 2018 (Issued in Exchange)	8-K	001-33357	4.3	December 7, 2016
4.7	First Supplemental to Indenture, dated as of July 24, 2017, by and among Protalix BioTherapeutics, Inc., the guarantors party thereto, The Bank of New York Mellon Trust Company, N.A., as trustee, and Wilmington Savings Fund Society, FSB, as collateral agent	8-K	001-33357	4.2	July 25, 2017
4.8	Second Supplemental Indenture, dated as of November 27, 2017, by and among Protalix BioTherapeutics, Inc., the guarantors party hereto and The Bank of New York Mellon Trust Company, N.A., as trustee, registrar, paying agent and conversion agent	8-K	001-33357	4.1	December 1, 2017
10.1	2006 Stock Incentive Plan, as amended	Def 14A	001-33357	Annex A	October 9, 2014
10.2	Employment Agreement between Protalix Ltd. and Yoseph Shaaltiel, dated as of September 1, 2004	8-K	001-33357	10.3	January 8, 2007
10.3	Employment Agreement between Protalix Ltd. and Einat Almon, dated as of December 19, 2004	8-K	001-33357	10.3	January 8, 2007
10.4	Employment Agreement between Protalix Ltd. and Yossi Maimon, dated as of October 15, 2006	8-K	001-33357	10.5	January 8, 2007
10.5	Lease Agreement between Protalix Ltd. and Angel Science Park (99) Ltd., dated as of October 28, 2003 as amended on April 18, 2005	8-K	001-33357	10.9	January 8, 2007
10.6	Unprotected Lease Agreement	10-K	001-33357	10.21	March 17, 2008
10.7	Employment Agreement by and between Protalix Ltd., and Tzvi Palash dated as of August 29, 2010	8-K	001-33357	10.1	September 7, 2010
10.8†	Amended and Restated Agreement between Protalix Ltd. and Comercio e Serviços Ltda. dated June 17, 2013	10-Q	001-33357	10.1	May 8, 2014
10.9†	Technology Transfer and Supply Agreement made as of June 18, 2013 by and between Protalix Ltd. and Fundação Oswaldo Cruz	10-Q	001-33357	10.3	May 8, 2014

10.10	Employment Agreement with Moshe Manor dated September 28, 2014	8-K	001-33357	10.1	September 29, 2014	
10.11†	Amended and Restated Exclusive License and Supply Agreement by and between Pfizer Inc. and Protalix Ltd., dated October 12, 2015	10-Q/A	001-33357	10.1	December 11, 2015	
10.12	Form of Note Purchase Agreement, dated of December 1, 2016 among Protalix BioTherapeutics, Inc. and the Purchasers	8-K	001-33357	10.1	December 7, 2016	
10.13	Form of Exchange Agreement, dated of December 1, 2016 among Protalix BioTherapeutics, Inc. and the Existing Holders	8-K	001-33357	10.2	December 7, 2016	
10.14	Form of U.S. Security Agreement, dated of December 7, 2016 among Protalix BioTherapeutics, Inc., the guarantors party thereto and Wilmington Savings Fund Society, FSB, as collateral agent	8-K	001-33357	10.3	December 7, 2016	
10.15	Form of Security Agreement/Debenture, dated of December 7, 2016 between Protalix BioTherapeutics, Inc. and Altshuler Shaham Trusts Ltd., as security trustee	8-K	001-33357	10.4	December 7, 2016	
10.16†	Exclusive License and Supply Agreement dated as of October 17, 2017, made by and between Protalix Ltd. and Chiesi Farmaceutici S.p.A.					X
21.1	Subsidiaries	10-K	001-33357	21.1	February 26, 2010	
23.1	Consent of Kesselman & Kesselman, Certified Public Accountants (Isr.), A member of PricewaterhouseCoopers International Limited, independent registered public accounting firm for the Registrant					X
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X

32.1	18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Certification of Chief Executive Officer	X
32.2	18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Certification of Chief Financial Officer	X
101.INS	XBRL INSTANCE FILE	X
101.SCH	XBRL SHEMA FILE	X
101.CAL	XBRL CALCULATION FILE	X
101.DEF	XBRL DEFINITION FILE	X
101.LAB	XBRL LABEL FILE	X
101.PRE	XBRL PRESENTATION FILE	X

† Portions of this exhibit were omitted and have been filed separately with the Secretary of the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment under Rule 24b-2 of the Exchange Act.

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, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, as of March 6, 2018.

PROTALIX
BIOTHERAPEUTICS,
INC.

By: /s/ Moshe Manor
Moshe Manor

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Moshe Manor and Yossi Maimon, and each of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution and re-substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that said attorneys-in-fact and agents, or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	**Title**	**Date**
/s/ Moshe Manor Moshe Manor	President, Chief Executive Officer (Principal Executive Officer) and Director	March 6, 2018
/s/ Yossi Maimon Yossi Maimon	Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer)	March 6, 2018

/s/ Shlomo Yanai Shlomo Yanai	Chairman of the Board	March 6, 2018
/s/ Amos Bar Shalev Amos Bar Shalev	Director	March 6, 2018
/s/ Zeev Bronfeld Zeev Bronfeld	Director	March 6, 2018
/s/ Yodfat Harel Buchris Yodfat Harel Buchris	Director	March 6, 2018
/s/ Aharon Schwartz Aharon Schwartz, Ph.D.	Director	March 6, 2018

PROTALIX BIOTHERAPEUTICS, INC.

CONSOLIDATED FINANCIAL STATEMENTS

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the board of directors and stockholders of

PROTALIX BIOTHERAPEUTICS, INC.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Protalix BioTherapeutics, Inc. and its subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations, changes in stockholders' equity (capital deficiency) and cash flows for each of the three years in the period ended December 31, 2017 including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2017 based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016 and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Kesselman & Kesselman, Trade Tower, 25 Hamered Street, Tel-Aviv 6812508, Israel, P.O Box 5005 Tel-Aviv 6150001 Telephone: +972 -3- 7954555, Fax:+972 -3- 7954556, www.pwc.co.il

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, 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.

/s/ Kesselman & Kesselman

Certified Public Accountants (Isr.)

A member of PricewaterhouseCoopers International Limited

Tel Aviv, Israel

March 6, 2018

We have served as the Company's auditor since 2000.

Kesselman & Kesselman, Trade Tower, 25 Hamered Street, Tel-Aviv 6812508, Israel, P.O Box 5005 Tel-Aviv 6150001 Telephone: +972 -3- 7954555, Fax:+972 -3- 7954556, www.pwc.co.il

PROTALIX BIOTHERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(U.S. dollars in thousands, except share and per share amounts)

	December 31,	
	2016	2017
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$63,281	$51,163
Accounts receivable – Trade	693	1,721
Other assets	2,648	1,934
Inventories	5,245	7,833
Total current assets	71,867	62,651
FUNDS IN RESPECT OF EMPLOYEE RIGHTS UPON RETIREMENT	1,677	1,887
PROPERTY AND EQUIPMENT, NET	8,703	7,676
Total assets	$82,247	$72,214
LIABILITIES NET OF CAPITAL DEFICIENCY		
CURRENT LIABILITIES:		
Accounts payable and accruals:		
Trade	$4,007	$7,521
Other	7,496	9,310
Convertible notes	53,872	5,921
Deferred revenues	837	
Total current liabilities	66,212	22,752
LONG TERM LIABILITIES:		
Convertible notes	19,343	46,267
Deferred revenues		26,851
Liability for employee rights upon retirement	2,348	2,586
Other long term liabilities	4,301	5,051
Total long term liabilities	25,992	80,755
Total liabilities	92,204	103,507
COMMITMENTS (Note 6)		
CAPITAL DEFICIENCY:		
Common Stock, $0.001 par value:	124	144
Authorized - as of December 31, 2016 and 2017, 250,000,000 shares; issued and outstanding, respectively - as of December 31, 2016 and 2017, 124,134,085 shares and 143,728,797		

shares, respectively		
Additional paid-in capital	202,575	266,495
Accumulated deficit	(212,656)	(297,932)
Total capital deficiency	(9,957)	(31,293)
Total liabilities net of capital deficiency	$82,247	$72,214

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

PROTALIX BIOTHERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(U.S. dollars in thousands, except share and per share amounts)

Year ended December 31,	
2015	2016