Protalix BioTherapeutics, Inc.
Form 10-K
March 13, 2014

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, 2013

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)

Florida	**65-0643773**
State or other jurisdiction	**(I.R.S. Employer**
of incorporation or organization	**Identification No.)**
2 Snunit Street	
Science Park	
POB 455	
	20100
Carmiel, Israel	
(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 MKT**

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. þ

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 ¨

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 28, 2013 was approximately $286 million (based upon a per share price equal to $4.91, the closing price for shares of the Registrant's common stock reported by the NYSE MKT for such date). Shares of common stock held by each officer, director and holder of 5% or more of the outstanding common stock have been excluded in that such persons may be

deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

On March 1, 2014, approximately 93,580,464 shares of the Registrant's common stock, par value $0.001 per share, were outstanding.

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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" and "intend" and words or phrases of similar import, as they relate to our 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:

- risks related to the commercialization efforts for taliglucerase alfa in the United States, Israel, Brazil and other countries;
- the risk of significant delays in the commercial introduction of taliglucerase alfa in the United States, Brazil, Israel and other markets as planned;
- risks related to the acceptance and use of taliglucerase alfa or any of our product candidates, if approved, by physicians, patients and third-party payors;

- our ability to supply drug product pursuant to our supply arrangement with the Brazilian Ministry of Health, or the Brazilian MOH;

- the risk that we will not be able to develop a successful sales and marketing organization for taliglucerase alfa in Israel or for any other product candidate in a timely manner, if at all;

- failure or delay in the commencement or completion of our preclinical studies and clinical trials which may be caused by several factors, including: unforeseen safety issues; determination of dosing issues; lack of effectiveness during clinical trials; slower than expected rates of patient recruitment; inability to monitor patients adequately during or after treatment; inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; 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 safety or efficacy, that our product candidates will not have the desired effects or includes undesirable side effects or other unexpected characteristics;

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

- delays in the approval or the potential rejection of any application filed with or submitted to the regulatory authorities reviewing taliglucerase alfa outside of the United States, Israel, Brazil and other countries in which taliglucerase alfa is already approved;

- our ability to establish and maintain strategic license, collaboration and distribution arrangements, and to manage our relationships with Pfizer Inc., with Fundação Oswaldo Cruz, or Fiocruz, an arm of the Brazilian MOH, or any other collaborator, distributor or partner;

- risks relating to our ability to finance our research programs, the expansion of our manufacturing capabilities and the ongoing costs in the case of delays in regulatory approvals for taliglucerase alfa outside of the United States, Israel, Brazil and other countries in which taliglucerase alfa is already approved;

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

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

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

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

- any lack of progress of our research and development activities and our clinical activities with respect to any product candidate;

- 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;

- risks relating to our ability to make scheduled payments of the principal of, to pay interest on or to refinance our 2018 convertible notes, or any other indebtedness;

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

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

· product liability risks;

· risks relating to biosimilar legislation and/or healthcare reform 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 foreign regulatory authorities may not accept or approve a marketing application filed by a pharmaceutical or biotechnology company for the drug product.

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, or ProCellEx. Using our ProCellEx system, we are developing a pipeline of proprietary, biobetter and biosimilar versions of recombinant therapeutic proteins, based on our plant cell-based expression technology, that primarily target large, established pharmaceutical markets and that rely upon known biological mechanisms of action. Our initial commercial focus has been on complex therapeutic proteins, including proteins for the treatment of genetic disorders, such as Gaucher disease and Fabry disease. We believe ProCellEx will enable us to develop proprietary recombinant proteins that are therapeutically equivalent or superior to existing recombinant proteins currently marketed for the same indications. Because we are primarily targeting biologically equivalent versions of highly active, well-tolerated and commercially successful therapeutic proteins, we believe our development process is associated with relatively less risk compared to other biopharmaceutical development processes for completely novel therapeutic proteins. We are now also applying the unique properties of our ProCellEx system for the oral delivery of therapeutic proteins, with the first two product candidates being glucocerebrosidase and antiTNF fusion protein.

The following table summarizes our current product and product candidates and their respective stages of development as of December 31, 2013.

On May 1, 2012, the U.S. Food and Drug Administration, or the FDA, approved for sale our first commercial product, taliglucerase alfa for injection, which is being marketed in the United States and Israel under the brand name ELELYSO™, as 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 by the Brazilian National Health Surveillance Agency (Agencia Nacional de Vigilancia Sanitaria, or ANVISA) in March 2013, by the Israeli Ministry of Health, or the Israeli MOH, in September 2012, and by the applicable regulatory authorities in Uruguay, Mexico and Chile. Taliglucerase alfa will be marketed under the name UPLYSO™ in Brazil and certain other Latin American countries. Taliglucerase alfa is our proprietary, recombinant form of glucocerebrosidase, or GCD, that is produced or expressed through ProCellEx. Taliglucerase alfa is the first plant cell-based recombinant therapeutic protein to be approved by the FDA or by the regulatory authorities with jurisdiction over any substantial market. Gaucher disease is a rare and serious lysosomal storage disorder with severe and debilitating symptoms. Gaucher patients suffer from mutations in or deficiencies of GCD, an enzyme that is naturally found in human cells.

Since May 2012, taliglucerase alfa has been marketed in the United States by Pfizer Inc., or Pfizer, our commercialization partner, as provided in the exclusive license and supply agreement by and between Protalix Ltd., our wholly-owned subsidiary, and Pfizer, which we refer to as the Pfizer Agreement. We granted Pfizer an exclusive, worldwide license to develop and commercialize taliglucerase alfa under the Pfizer Agreement, but we retained those rights in Israel and in Brazil. We have agreed to a specific allocation between Protalix Ltd. and Pfizer of the

responsibilities for the continued development efforts for taliglucerase alfa outside of Israel. Since 2013, taliglucerase alfa has been marketed in Israel by Protalix Ltd.

On June 18, 2013, we entered into a Supply and Technology Transfer Agreement, or the Brazil Agreement, with Fiocruz, for taliglucerase alfa. The 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. Under the agreement, Fiocruz has committed to purchase at least approximately $40 million worth of taliglucerase alfa during the first two years of the term. In subsequent years, Fiocruz is required to purchase at least approximately $40 million worth of taliglucerase alfa per year. Additionally, we are not required to complete the final stage of the technology transfer until Fiocruz purchases at least approximately $280 million worth of taliglucerase alfa.

We are cooperating with Pfizer to obtain marketing approval for taliglucerase alfa in additional countries and jurisdictions. In addition to those countries in which taliglucerase alfa has been approved, marketing authorization applications have been filed in other countries.

In December 2012, we entered into a Clinical Development Agreement with Pfizer under which we will continue to manage, administer and sponsor current, ongoing clinical trials relating to ELELYSO. We are currently sponsoring extension studies of ELELYSO in adult and pediatric patients. New clinical trials for ELELYSO, if it is elected that any such clinical trial be performed, will be conducted and sponsored by Pfizer. Under the terms of the agreement, we were eligible to receive a payment of $8.3 million upon the achievement of certain near-term clinical development goals. The goals were achieved prior to the end of fiscal year 2012 and the $8.3 million payment has been paid in full. This agreement helps to maintain the continuity of the ongoing clinical trials for Gaucher patients and physicians and reinforces the companies' mutual commitment to the Gaucher community.

We performed a number of studies on taliglucerase alfa to supplement the pivotal phase III clinical trial, which we completed in September 2009. We initiated a double-blind, follow-on extension study in 2008 which consisted of eligible patients who had completed nine months of treatment in the pivotal phase III clinical trial. The patients were offered the opportunity to continue to receive taliglucerase alfa at the same dose they received in the pivotal trial for an additional 15 months in a blinded manner. We also conducted a nine-month, worldwide, multi-center, open-label, switch-over clinical study evaluating the safety and efficacy of switching Gaucher patients currently treated with Cerezyme®, which is produced by Genzyme Corporation, or Genzyme (a Sanofi company), with taliglucerase alfa, which was successfully completed in 2011. We also conducted a 12-month clinical trial of naïve and switchover pediatric patients, which was successfully completed in 2012. Based on the data from this study, an application for a supplement to the NDA for ELEYSO, allowing a pediatric use indication to be added to the product label, has recently been submitted by Pfizer to the FDA. Patients in the extension trials are still being treated with taliglucerase alfa.

Currently, patients are being treated with taliglucerase alfa on a commercial basis in the United States, Brazil, Israel and Chile. Globally, patients are being treated through our extension trials and related studies, compassionate use programs, special access agreements, named patient provisions and other programs designed to ensure that treatments are available to Gaucher patients in light of recent shortages of approved treatments. In France, Gaucher patients are being treated with taliglucerase alfa through an Autorisation Temporaire d'Utilisation (ATU), or Temporary

Authorization for Use, a regulatory mechanism used by the French Health Products and Safety Agency to make non-approved drugs available to patients in France when a genuine public health need exists. In addition to the United States and France, taliglucerase alfa is currently being provided to Gaucher patients under special access agreements or named patient provisions in Brazil and in other countries. Hundreds of patients, in the aggregate, have been treated with taliglucerase alfa.

In addition to taliglucerase alfa, we are developing an innovative product pipeline using our ProCellEx protein expression system. Our product pipeline currently includes, among other candidates: PRX-102, a therapeutic protein candidate for the treatment of Fabry disease; PRX-112, an orally administered glucocerebrosidase enzyme for the treatment of Gaucher patients utilizing oral delivery of the recombinant GCD enzyme produced and encapsulated within carrot cells; PRX-106, an oral antiTNF, a plant cell expressed recombinant fusion protein combined of the binding domain of the human TNF receptor (TNFR) and an antibody portion, which is being developed for the treatment of certain immune and inflammatory diseases, such as rheumatoid arthritis, colitis, Crohn’s disease, psoriasis and other autoimmune and inflammatory disorders; PRX-110, a proprietary plant cell recombinant human Deoxyribonuclease 1 under development for the treatment of Cystic Fibrosis, to be administered by inhalation; PRX-107, a proprietary plant cell recombinant human Alpha1-antitrypsin, or AAT, and others.

Except for the rights to commercialize taliglucerase alfa worldwide (other than Brazil and Israel), which we licensed to Pfizer, we hold the worldwide commercialization rights to all of our proprietary development candidates. We have built an internal marketing team designed to serve the Israeli market for taliglucerase alfa and we intend to establish internal commercialization and marketing teams for our other product candidates in North America, the European Union and in other significant markets, including Israel, subject to required marketing approvals, as the need arises. In addition, we continuously evaluate potential strategic marketing partnerships as well as collaboration programs with biotechnology and pharmaceutical companies and academic research institutes.

Industry Overview

Recombinant proteins have revolutionized the treatment of a variety of diseases and disorders. Recombinant proteins are forms of human proteins that are produced, or expressed, using a mammalian, plant, bacterial or yeast cell as a production engine. In the early 1970s, a number of key scientific breakthroughs, including, among others, the demonstration of genetic engineering and genetic sequencing techniques, as well as the synthesis of genes, led to the advancement of recombinant protein technology. As a result, the market for pharmaceutical therapeutics has undergone a transformation as recombinant proteins and other biologic products have become an increasingly significant portion of the global drug market and the focus of research worldwide. The IMS Institute for Healthcare Informatics reports that global biologic spending was $157 billion in 2010 (Report by the IMS Institute for Healthcare Informatics, July 2012).

Mammalian cell-based systems are the current industry standard for expression of recombinant therapeutic glycoproteins (complex proteins that contain sugar residues), including catalytic enzymes and monoclonal antibodies. Mammalian cell-based systems were first introduced in the late 1980s and are currently used to produce many of the biotechnology industry's largest and most successful therapeutic proteins, including Epogen®, Neupogen®, Cerezyme, Rituxan®, Enbrel, Neulasta®, Remicade and Herceptin®. 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. The cells most often used in connection with mammalian cell-based protein expression are Chinese hamster ovary (CHO) cells.

Mammalian cell-based expression 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). 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. Due to their significant advantages, 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.

Despite the utility and widespread use of mammalian cell-based systems, they are subject to a number of disadvantages. CHO cells and other mammalian cells are highly sensitive and can only be grown under near perfect conditions, requiring highly complex, expensive, stainless steel bioreactors which tightly regulate the required temperature, pH and oxygen levels. As a result, such bioreactor systems are very costly and complicated to operate. CHO cells and other mammalian cells are also susceptible to viral infections, including human viruses, and several

cases of viral contamination have occurred recently. 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. In addition, mammalian cell-based expression systems require large quantities of sophisticated and expensive growth medium to accelerate the expression process.

Several companies and research institutions have explored alternatives to mammalian cell-based production technologies that overcome some of these disadvantages, focusing primarily on 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.

ProCellEx: Our Proprietary Protein Expression System

ProCellEx is our proprietary production system. We have developed ProCellEx based on our plant cell culture technology for the development, expression and manufacture of recombinant proteins. ProCellEx 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 protein expression system does not involve mammalian or animal components or transgenic field-grown, whole plants at any point in the production process. As a result, through our ProCellEx protein expression system, we believe that we can develop recombinant therapeutic proteins yielding substantial cost advantages, accelerated development and other competitive benefits when compared to mammalian cell-based protein expression systems.

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 the ProCellEx system will 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: the FDA's approval of taliglucerase alfa; the clinical and preclinical studies we have performed to date, including the positive efficacy and safety data in our phase III study of taliglucerase alfa, our switchover study and our extension study; preclinical results in well-known models in our enzyme for each of Fabry disease and pr-antiTNF; extensive animal studies for our PRX 106 enzyme; and 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 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.

We are also using our ProCellEx system to produce active recombinant proteins systemically through oral administration of plant cells expressing biotherapeutic proteins. In such method, an enzyme is naturally encapsulated within carrot 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 the enzyme in active form to the bloodstream. With initial proof of concept now demonstrated, 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 anti TNF, and a phase I clinical trial of oral GCD in Gaucher patients.

To date, our manufacturing facility, in which we utilize our ProCellEx system, was determined to be acceptable by each of the FDA, 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 believe that our ProCellEx protein expression system, including our advanced genetic engineering technology and plant cell-based protein expression methods, affords us a number of significant advantages over mammalian, bacterial, yeast and transgenic cell-based expression technologies, including the following:

Ability to Penetrate Certain Patent-Protected Markets. We seek to develop recombinant proteins that we believe we can produce and commercialize without infringing upon 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 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, PRX-102 and certain of our other product candidates.

Significantly Lower Capital and Production Costs. Plant cells have a number of dynamic qualities that make them well-suited for the production of therapeutic proteins. Plant cells grow rapidly under a variety of conditions and are not as sensitive to temperature, pH and oxygen levels as are mammalian cells. Our ProCellEx system, therefore, requires significantly less upfront capital expenditures as it does not use 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. We believe that these factors will potentially result in lower capital and production costs for the commercial scale production of proteins by our ProCellEx system thereby providing us with a competitive advantage over competing protein expression technologies.

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. As a result, the risk of contamination of our products under development and the potential risk of viral transmission from our products 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 our ProCellEx system compared to mammalian cell-based expression systems.

Efficient Production Relative to Mammalian Based Systems. Our ProCellEx protein expression system produces enzymes which 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, including the proteins for the treatment of Gaucher disease. 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. For example, in the production of Cerezyme, exposing these terminal mannose sugar residues involves a multitude of highly technical steps which add time and cost to the production process. 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. Our ProCellEx protein expression system, by contrast, produces taliglucerase alfa in a “ready to use” form that does not require additional glycosilation or other modifications to make taliglucerase alfa suitable for use as an ERT for Gaucher disease. 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.

Broad Range of Expression Capabilities. Our ProCellEx protein expression system is able to produce a broad array of complex glycosilated proteins, which differentiates our system from bacterial and yeast cell-based systems which are unable to produce complex proteins. 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.

Potential ability to administer active therapeutic enzymes orally. We are using our ProCellEx system to produce active recombinant proteins systemically through oral administration of plant cells expressing biotherapeutic proteins. 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, 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 anti TNF, and a phase I clinical trial of oral GCD in Gaucher patients.

Our Strategy

Our goal is to become a leading fully integrated biopharmaceutical company focused on the development and commercialization of proprietary biobetter and biosimilar versions of recombinant therapeutic proteins. To achieve our goal, we intend to:

Commercialization of ELELYSO in Israel/UPLYSO in Brazil. We intend to maximize our supply and technology agreement in Brazil to potentially generate significant revenues in the territory for which we own the rights. We also intend to continue to work closely with the Israeli HMOs to increase our revenues in our home country.

Facilitate the successful development and commercialization of ELELYSO by Pfizer. We intend to work closely with our commercialization partner, Pfizer, to continue to develop and to commercialize ELELYSO. We have facilitated relationships between Pfizer and the Gaucher community and third-party payors.

Obtain Regulatory Approval for ELEYSO for the Treatment of Gaucher Disease. ELELYSO has been approved for marketing in the United States, Israel, Brazil, Uruguay, Mexico and Chile. In addition, Pfizer has submitted marketing applications to the regulatory authorities of other countries.

Establish Development and Commercialization Alliances with Corporate Partners. We believe that our technology and know-how has broad applicability to many classes of proteins and can be used to develop and potentially enhance numerous existing marketed protein therapeutics. We continuously review a broad array of product partnering, technology sharing and other strategic alternatives and expect that such transactions will facilitate the leveraging of our technology and know-how to optimize our resources and effectively penetrate a wider range of target diseases and therapeutic markets.

Develop PRX-102 and Oral Glucocerebrosidase. In December 2012, the first patient was treated in our phase I/II clinical trial of Fabry patients with PRX-102 and, in February 2014 we reported phase I clinical trial results for our phase I clinical trial of Oral GCD in Gaucher patients, including patients with low platelet counts, at the Lysosomal Storage Disease Network WORLD Symposium (LDN WORLD). We expect to initiate next phase clinical trial of Oral GCD in the second half of 2014.

Develop a Pipeline of Innovative and Biosimilar Versions of Recombinant Therapeutic Proteins. We are leveraging our ProCellEx protein expression system to develop a pipeline of innovative or biosimilar versions of recombinant proteins, with an emphasis on therapeutic treatments with large market opportunities. We select additional therapeutic candidates for development through in-house testing, licensing agreements with academic institutions and collaborations with pharmaceutical partners. We have currently identified several product candidates that are mainly oriented towards the specialty disease and therapeutic market segments, including PRX-102, our product candidate for Fabry disease, and our orally-administered glucocerebrosidase enzyme. We have also identified several other product candidates that are chemical equivalents of approved therapeutic products that will no longer be patent protected within the next couple of years, such as oral-antiTNF, our proprietary product candidate for the treatment of certain immune diseases such as rheumatoid arthritis, colitis, Crohn’s disease, psoriasis and other autoimmune and inflammatory disorders. In addition, we have a number of other proteins in different stages of research and development in our pipeline. We believe our cost-effective technology will be an important asset for the commercialization of such drug candidates. We believe that the clinical and regulatory pathway for many of our pipeline product programs candidates is already established, which may reduce the risks and costs associated with our clinical development programs. Furthermore, established markets already exist for the development of most of our current product candidates.

Collaborate with Third Party Pharmaceutical Companies and Build a Targeted Sales and Marketing Infrastructure. We have licensed to Pfizer the right to commercialize ELELYSO worldwide, except in Israel and Brazil. We have built our own, internal marketing team designed to serve the Israeli market for ELELYSO and we intend to establish similar sales and marketing capabilities for our other product candidates in North America, the European Union and in other significant markets, including Israel. We believe that the focus of our current clinical pipeline mainly on relatively rare genetic disorders with small patient populations and a highly concentrated group of physicians focused on treating patients with such disorders will facilitate our creation of a targeted internal sales force. In addition we are continuously evaluating potential strategic marketing partnerships with respect to our other product candidates.

Acquire or In-License New Technologies, Products or Companies. We continuously seek attractive product candidates and innovative technologies to in-license or acquire. We intend to focus on product candidates that would be synergistic with our ProCellEx protein expression system and expertise and that represent large potential market opportunities. We believe that by pursuing selective acquisitions of technologies in businesses that complement our own, we will be able to enhance our competitiveness and strengthen our market position. We are evaluating several such products, and we engaged in confidential discussions with a number of academic and medical institutes for these matters.

Leverage Strength and Experience of Our Management Team and Board of Directors. Our management team has extensive experience in the biotechnology and pharmaceutical industry. Our director, Professor Roger D. Kornberg, who heads our Scientific Advisory Board, is a renowned biochemist and laureate of the Nobel Prize in Chemistry. We intend to continue to leverage their experience and established track record as well as their relationships across the biotechnology and pharmaceutical industries.

Leverage Our ProCellEx System to Potentially Enable the Oral Administration of Active Therapeutic Enzymes. 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. We intend to explore additional therapeutic indications which can be produced through our proprietary technology.

ELELYSO, Our First Commercial Product

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 in September 2012, the Brazilian National Health Surveillance Agency (ANVISA) in March 2013, the Mexican Federal Commission for the Protection against Sanitary Risk (COFEPRIS) in April 2013 and the regulatory authorities of other countries.

We believe that taliglucerase alfa has the potential to offer patients and healthcare payors a more effective and cost efficient treatment of Gaucher disease compared to the currently available ERTs.

Although Gaucher disease is a relatively rare disease, it represents a substantial commercial market due to the severity of the symptoms and the chronic nature of the disease. We believe that the approval of taliglucerase alfa as a treatment for Gaucher disease with its potentially longer acting profile and more cost-effective development process, may lead to an increase in the number of patients who will be able to have access to and afford such treatment, thereby expanding the size of the market for Gaucher disease treatments.

Gaucher Disease Background

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). The normal degradation products of GlcCer are glucose and ceramide, which are easily excreted by the cells through normal biological processes. Patients with Gaucher disease lack or otherwise have dysfunctional GCD and, accordingly, are not able to break down GlcCer. The absence of an active GCD enzyme leads to the accumulation of GlcCer in lysosomes of certain white blood cells called macrophages. Macrophages affected by the disease become highly enlarged due to the accumulation of GlcCer and are referred to as “Gaucher cells.” Gaucher 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.

Current Treatments for Gaucher Disease

The standard of care for Gaucher disease is enzyme replacement therapy using recombinant GCD to replace the mutated or deficient natural GCD enzyme. It is estimated that there are approximately 12,000 people suffering from Gaucher disease worldwide, but only approximately 6,000 patients are undergoing treatment. 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, enzyme replacement therapies commercialized by Genzyme and Shire, respectively, are the only recombinant GCDs currently available on the market for the treatment of Gaucher disease. As enzyme replacement therapy does not cure the genetic disorder, but rather provides an external source for transfusion of the missing or mutated enzyme, Gaucher patients generally receive the treatment over their entire lifetime. According to public reports by Sanofi, consolidated sales of Cerezyme during the year ended December 31, 2013 were €688 million (or approximately $950 million), a growth of approximately 14% compared to the same period in 2012. Shire reported annual worldwide sales of VPRIV of approximately $343 million in 2013, a growth of 12% compared to VPRIV’s sales in 2012.

Cerezyme is produced through a mammalian cell-based protein expression process in CHO cells and VPRIV is produced using a human cancer cell line. There are no known severe side effects to the use of Cerezyme or VPRIV, and Cerezyme’s approved use over the past decade suggests that it is an effective treatment of Gaucher disease. However, Cerezyme and VPRIV are both subject to the limitations of most mammalian cell-based therapeutic proteins, including lengthy and costly production processes and contamination risks.

Zavesca (miglustat), which is marketed by Actelion Ltd., or Actelion, 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, Zavesca's use has been limited with respect to treating Gaucher disease. However, Zavesca is also used to treat other rare disorders. Actelion has reported total sales of Zavesca of approximately CHF 96 million (approximately $109 million) in 2013, an increase of approximately 13% compared to sales in 2012.

Taliglucerase Alfa Development Program

We completed a phase I clinical trial in 2006 and, after discussions with the FDA, we proceeded directly with a pivotal phase III clinical trial of taliglucerase alfa without undergoing a phase II clinical trial. We reported positive top-line results of the phase III clinical trial in October 2009 and full study results in February 2010. This study was summarized in a publication in BLOOD, the Journal of the American Hematological Society (Zimran, et. al., September 2011).

Phase III Clinical Trial and Related Studies

We initiated enrollment and treatment of naive patients in our phase III clinical trial in 2007, after having reached an agreement with the FDA regarding the design of the study through the FDA's special protocol assessment (SPA) process. Consistent with the SPA, the phase III clinical trial was a multi-center, world-wide, randomized, double-blind, parallel group, dose-ranging study to assess the safety and efficacy of taliglucerase alfa in 31 treatment-naive patients suffering from Gaucher disease. In the trial, patients were selected randomly for one of two dosing arms (60 U/kg or 30 U/kg) and received intravenous infusions of taliglucerase alfa once every two weeks for a nine-month period. The primary endpoint of the study was a 20% mean reduction from baseline in spleen volume after nine months, as measured by MRI. Major secondary endpoints were an increase in hemoglobin, decrease in liver volume and increase in platelet count. Patients enrolled in the trial were treated in 11 selected leading medical centers throughout Europe, Israel, North America, South America and South Africa. Enrollment was completed in the fourth quarter of 2008 and the trial was successfully completed in September 2009.

During the third quarter of 2008, we initiated a double blind, follow-on extension study as part of our phase III clinical trial. Eligible patients who successfully completed nine months of treatment in our phase III clinical trial were offered the opportunity to participate in the extension study and to continue to receive taliglucerase alfa at the same dose they received in the phase III clinical trial for an additional 15 months in a blinded manner. Accordingly, the extension trial included two treatment groups; one treated with a 60 U/kg dose and the other with a 30 U/kg dose. The major endpoints of the study were spleen volume, liver volume, hemoglobin concentration, platelet count, and chitotriosidase activity. Twenty-six patients were originally enrolled in the extension trial which was performed in centers throughout Europe, Israel, North America, South America and South Africa. Three of the 26 patients enrolled in the extension trial discontinued treatment; one switched to our compassionate use program, one was unable to comply with study protocol and one had a skin reaction during month 15. We also initiated a home care treatment program for patients enrolled in the extension study.

In addition, in the fourth quarter of 2008, we announced the enrollment of the first patient in a worldwide, multi-center, open-label, switch-over trial to assess the safety and efficacy of taliglucerase alfa. The switch-over trial, which was not a prerequisite for approval, was originally designed to include 15 Gaucher patients that were currently undergoing ERT with imiglucerase (Cerezyme). Due to the shortage of Cerezyme in 2009, after fully enrolling 15 patients, we extended the trial to include additional patients. A total of 26 adult patients were enrolled in the switchover trial. Patients enrolled in the trial were switched from imiglucerase (doses ranging from approximately 10-60 U/kg every other week) to an equivalent dose using the same number of units of taliglucerase alfa over a nine-month period.

In 2010 we initiated a clinical trial of naïve pediatric patients which we completed in 2012. Eleven treatment-naive patients with symptoms and clinical manifestations of Gaucher disease between the ages of two and eighteen were enrolled in the trial. Patients were randomized to receive two different doses in a blinded manner; five patients were treated with a 60 U/kg dose and six patients were treated with a 30 U/kg dose. The primary endpoint of the study was change in hemoglobin concentration, and the secondary endpoints were change of spleen volume, liver volume, platelet count and chitotriosidase activity. Patients were enrolled in clinics in Israel, Paraguay, and South Africa.

Results of our Phase III Clinical Trial and Extension Trial

We reported positive top-line results of our phase III clinical trial of taliglucerase alfa in October 2009 and full study results in February 2010. In the clinical trial, taliglucerase alfa significantly reduced mean spleen volume after nine months compared with baseline in both treatment groups, thereby meeting the trial's primary endpoint of reduced mean spleen volume after nine months. In February 2013, we announced interim data from 23 adult patients enrolled in our extension trial. According to the interim data, after 36 months (nine months in the phase III clinical trial and 27 months in the extension trial), patients continued to demonstrate a significant improvement in all parameters with a similar safety profile as seen in the phase III clinical trial.

In the phase III clinical trial, the 60 U/kg group demonstrated a statistically significant mean reduction in spleen volume of 38.0% ($p<0.0001$) and the 30 U/kg group demonstrated a significant mean reduction in spleen volume of 26.9% ($p<0.0001$). In addition, the primary endpoint was achieved in both treatment groups after only six months of therapy. Patients treated with taliglucerase alfa in the extension trial continued to demonstrate a statistically significant reduction in mean spleen volume after 36 months, compared with baseline, in both treatment groups; reductions of 62.0% in the 60 U/kg group and of 47.0% in the 30 U/kg group.

Statistically significant improvements were also observed for the secondary endpoints of the phase III clinical trial, including increase in hemoglobin level, decrease in liver size and increase in platelet count, after nine months when compared to baseline for the 60 U/kg dose. These improvements continued in the extension trial. Patients in both dosage groups demonstrated mean increases in hemoglobin from baseline; mean increases from 11.4 g/DL to 13.6 g/DL ($p<0.0001$) (22.2%) in the 60 U/kg group and from 12.2 g/DL to 14.0 g/DL ($p<0.0010$) (14.8%). In the extension trial, at 36 months, clinically significant mean increases in hemoglobin concentration were also demonstrated by both groups; mean increases from baseline, from 11.0 g/DL to 14.0 g/DL (27.3%), in the 60 U/kg group and mean increases from baseline, from 12.4 g/DL to 14.3 g/DL (15.3%), in the 30 U/kg group. Patients with anemia demonstrated a mean increase from baseline in hemoglobin concentration, from 9.5 g/DL to 13.1 g/DL (37.9%); patients with normal hemoglobin show a mean increase of 10.3% in hemoglobin, from 13.6 g/DL at baseline to 15.0 g/DL after 36 months of treatment.

In the phase III clinical trial, patients in both dosage groups demonstrated mean decrease (reduction) in liver volume; reductions of 11.1% ($p<0.0001$) in the 60 U/kg group and of 10.48% ($p<0.0041$) in the 30 U/kg group. In the extension trial, at 36 months, both groups demonstrated clinically significant mean reductions in liver volume; reductions of 19.0% in the 60 U/kg group and of 21.0% in the 30 U/kg group; patients with Hepatomegaly demonstrated a reduction in liver volume of 30.0% in the 60 U/kg group and of 22.0% in the 30 U/kg group.

In the phase III clinical trial, patients in both dosage groups demonstrated mean increases in platelet count; an increase in platelet count of 41,494 ml or 72.1% (p=0.0031) in the 60 U/kg group, and a nominal increase of 11,427 ml or 13.7% (p=0.0460) in the 30 U/kg group. Accordingly, the lower dose group did not meet the secondary endpoint relating to platelet count. In the extension trial, at 36 months, both groups demonstrated clinically significant mean increases in platelet count; increases from 73,055 to 136,027 in the 60 U/kg group and from 64,900 to 94,683 in the 30 U/kg group.

Last, 30 patients in the phase III clinical trial had chitotriosidase measurements, a biomarker of Gaucher disease. In these patients, chitotriosidase decreased from baseline in both the 30U/kg and 60U/kg groups by 47.3% and 58.4%, respectively. In the extension trial, at 36 months, mean reductions in chitotriosidase activity were demonstrated by both groups; a reduction of 83.0% in the 60 U/kg group and of 73.5% in the 30 U/kg group.

The safety analysis for both treatment groups in the phase III clinical trial showed that taliglucerase alfa was well tolerated and no serious or severe adverse events were reported. The safety analysis in the extension trial for both treatment groups at 36 months also demonstrates that taliglucerase alfa was well tolerated, and no drug related serious adverse events were reported.

In the phase III clinical trial, no serious related adverse event was reported and most of the adverse events were considered unrelated to taliglucerase alfa. The most frequent mild to moderate adverse event was headache. Other mild to moderate adverse events included dizziness, muscle spasm, chest discomfort, nausea, skin irritation and arthalgia. Adverse events in the extension trial included headache, pruritus, hypersensitivity, abdominal pain, fixed drug eruption, arthalgia and infusion related reactions (dizziness, chills, nausea).

Results of Our Switchover Trial; Long Term Data

In November 2010, we announced positive preliminary data from the first 15 patients that completed our switchover trial of taliglucerase alfa, and in February 2012 we reported full results from 25 adult patients in the trial. In February 2013, we announced interim results from an extension trial related to the switchover trial at 36 months. The results of the first trial demonstrate that over a nine-month treatment period of the study, patients remained stable with regard to all of the efficacy endpoints (hemoglobin concentration, platelet count, spleen and liver volume) and chitotriosidase activity after switching to taliglucerase alfa from imiglucerase. The safety analysis presented for the switchover trial demonstrates that taliglucerase alfa was well tolerated, and no drug related serious adverse events were reported. Additionally, all drug-related adverse effects were mild or moderate and transient in nature.

Nineteen of the 25 patients in the switchover trial elected to continue to be treated in an extension trial for an additional 12 months. Five of the six patients that did not proceed to the extension trial continued to be treated with

taliglucerase alfa through our compassionate use program; one patient was unable to comply with the extension study protocol and therefore was unable to participate. A 24-month interim analysis of the switchover trial demonstrates that patients remained stable with regard to all of the efficacy endpoints and chitotriosidase activity after switching to taliglucerase alfa from imiglucerase. The safety analysis presented for the extended switchover trial demonstrates that taliglucerase alfa was well tolerated, and no drug related serious adverse events were reported. Four of the nineteen patients enrolled in the extension trial discontinued treatment; one switched to our compassionate use program, one enrolled in another clinical trial, one was unable to comply with study protocol and one was not pleased with that individual's personal results. In conclusion, the data demonstrates that taliglucerase alfa has a well-established safety profile and is an effective alternative treatment for adult Gaucher patients previously treated with imiglucerase.

Results of Our Pediatric Trial

In July 2012, we announced data from our clinical trial of taliglucerase alfa in pediatric Gaucher patients. After 12 months of treatment with taliglucerase alfa, changes in hemoglobin concentration were demonstrated by both dosage groups, with increases of 15.8% in the 60 U/kg group and of 13.8% in the 30 U/kg group. In addition, significant improvements were also seen in all secondary endpoints. Spleen volumes decreased by 41.1% in patients receiving 60 U/kg, and by 28.6% in patients receiving 30 U/kg of taliglucerase alfa. Similarly, liver volumes decreased by 14.0% in the 60 U/kg group and 6.3% in the 30 U/kg group. Both treatment groups also demonstrated improvements in platelet counts with a 73.7% increase from baseline in the 60 U/kg group, and a 30.9% increase from baseline in the 30 U/kg group. Lastly, the chitotriosidase activity decreased from baseline, with a 66.0% reduction in patients receiving 60 U/kg and a 58.0% reduction in patients receiving 30 U/kg. The majority of the treatment-related adverse events were mild or moderate in intensity, and transient in nature. One severe adverse event was assessed as treatment-related; gastroenteritis. The event was reported as serious due to the need for hospitalization for rehydration. This patient continues to receive taliglucerase alfa. Subsequently, Pfizer submitted to the FDA a supplemental request to the ELEYSO NDA covering the treatment of pediatric Gaucher patients.

Long-Term Bone Marrow Responses

As bone disease is one of the most debilitating features of Gaucher disease, quantification of bone marrow involvement is important for monitoring the response to treatment. Therefore, our phase III clinical trial and the extension trial included bone marrow fat fraction (Ff) measured by quantitative chemical shift imaging (QCSI) as an exploratory parameter to evaluate bone marrow response in eight treatment naïve Gaucher patients with intact spleens that participated in the trials. Ff results were compared to outcomes in 15 untreated Dutch Gaucher patients with a follow-up interval of one year. Five taliglucerase alfa treated patients had a Ff below the threshold that relates to complication risk (<0.23) at baseline (median (n=8) 0.19, range 0.11–0.35). Ff significantly increased compared to baseline (p=0.012) and compared to untreated patients (p=0.005), already after one year of follow-up with further improvement up to 36 months. In four patients with the lowest Ff, the higher dose resulted in increases above 0.23 within one year. All eight patients had sustained improvements in all other parameters. There was no influence of antibodies on response parameters. This data demonstrates that treatment with taliglucerase alfa results in significant increases in lumbar spine fat fractions, which indicates clearance of Gaucher cells from the bone marrow.

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 an 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. We believe that the treatment of Fabry disease is a specialty clinical niche with the potential for high growth.

Fabry Disease Background

Fabry disease is characterized by subnormal or absent enzymatic activity of alpha-GAL-A, a lysosomal enzyme which primarily catalyses the hydrolysis of terminal alpha-galactosyl groups of glycolipids, mainly the glycosphingolipid globotriaosylceramide (Gb3). The accumulation of Gb3 in body tissues results in Fabry disease. The ultimate consequence of glycosphingolipid deposition in the vasculature and other tissues is end-organ failure, particularly of the kidney, but also of the heart and cerebrovascular system. In addition, involvement of the central, peripheral and autonomic nervous systems results in episodes of pain and impaired peripheral sensation. Fabry disease affects approximately 8,000 people globally. In PRX-102, the prh-alpha-GALA, naturally occurring as a homodimer, is

PEGylated and cross-linked to support and reinforce the homodimeric structure, which is crucial for the enzymatic activity of this enzyme. PRX-102 has been shown to be taken up by Fabry patients' cells where it localizes to the lysosome, in which Gb3 accumulates. PRX-102 is characterized by higher stability under physiologically relevant conditions, and extended circulation residence time as compared to current ERTs for Fabry disease.

Current Treatments for Fabry Disease

Currently there are two drugs available on the market to treat Fabry disease. Fabrazyme, marketed by Genzyme, is approved for the treatment of Fabry disease in the United States and the European Union. Sanofi reported €383 million (approximately $509 million) in worldwide sales of Fabrazyme in 2013, a growth of 39% compared to 2012. The other approved drug for the treatment of Fabry disease in the European Union is Replagal, which is marketed by Shire. Shire reported $467.9 million in sales of Replagal in 2013, a decline of 6% compared to 2012. According to public reports by Shire, during 2012 Shire withdrew its Biologics License Application (BLA) for Replagal with the FDA.

PRX-102 Development Program

PRX-102 has demonstrated a significantly longer circular half-life than that of Replagal, over 40 times greater. In preclinical tests, we compared enzymatic activity of both PRX-102 and Replagal in human plasma and found that Replagal had a 13 minute half-life compared to a half-life of 581 minutes for PRX-102. See Figure 1.

Figure 1. Enhanced Circulatory Half-Life

In addition to the significantly greater half-life, our animal studies of PRX-102 demonstrate that the enzyme exhibits higher activity levels in target organs over time in Fabry mice after a single injection. See Figures 2 and 3.

Figure 2. Improved In-vivo Activity in Heart **Figure 3. Improved In-vivo Activity in Kidney**

In December 2012, the first patient was treated with PRX-102 in our phase I/II clinical trial of Fabry patients. The phase I/II clinical trial is a worldwide, multi-center, open label, dose ranging study to evaluate the safety, tolerability, pharmacokinetics and exploratory efficacy parameters of PRX-102 in adult Fabry patients. The trial is designed to enroll 18 adult Fabry patients, each in one of three dosing groups. Each patient will receive intravenous infusions of PRX-102 every two weeks for 12 weeks. After the completion of the protocol, we intend to offer enrolled trial patients the option to continue to receive PRX-102 in an open-label extension study.

Based on the pre IND meeting we held with the FDA in 2010, our experience with taliglucerase alfa and the experience of other companies developing ERTs for Fabry disease, we have reason to believe that, if favorable data is accumulated in our phase I/II clinical trial, the FDA may allow us to proceed directly with a pivotal phase III clinical trial. However, there can be no assurance that we will successfully complete our phase I/II clinical trial and if we do, that the trial will result in favorable data. In addition, there can be no assurance that the FDA will allow us to proceed directly with a phase III clinical trial after completion of our phase I/II clinical trial.

In pre-clinical studies, PRX-102 demonstrated preliminary efficacy in a Fabry animal model. Chemical modifications made to PRX-102 improved the enzyme’s activity and stability resulting in prolonged activity profiles and enhanced bioavailability in animals. The modifications also have the potential to decrease the immunogenicity of the enzyme, which is a major drawback of currently approved therapies for Fabry disease.

PRX-112; Orally Administered GCD for the Treatment of Gaucher Disease

We are developing PRX-112, an orally-delivered glucocerebrosidase (GCD) enzyme for the potential enzyme replacement therapy treatment of Gaucher disease. This is representative of a potential method for delivering active recombinant proteins systemically through oral administration of plant cells expressing biotherapeutic proteins. Oral GCD is a plant cell-expressed form of GCD that is naturally encapsulated within carrot cells genetically engineered to express the GCD 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 GCD would be the first protein to be administered orally rather than through intravenous therapy.

We believe that oral delivery of GCD presents a number of advantages. First, oral GCD consists of the same transformed genetically modified carrot plant root cells expressing prGCD from which we derive the active drug substance taliglucerase alfa. Therefore, it has the advantage of leveraging the well-characterized mechanism of action of our intravenously-administered taliglucerase alfa product. In addition, daily dosing of GCD provides potentially better clinical benefit and improved PK profile than the current, once every two weeks IV bolus of enzyme. We expect that providing Gaucher patients with a constant and continuous supply of this housekeeping enzyme should demonstrate a greater physiological effect compared to bolus delivery of enzyme via IV therapy. We also expect that raising the non-sufficient endogenous enzyme levels in Gaucher patients to levels of active enzyme present in the circulation, should be sufficient to prevent accumulation of the substrate. For these reasons, we believe that oral delivery of GCD may dramatically change the treatment paradigm for Gaucher patients, compared to the intravenous delivery of taliglucerase alfa, and contribute to increased compliance and the facilitation of treatment management.

Our oral taliglucerase alfa product candidate is a recombinant form of the GCD enzyme, not a small molecule. This differentiates our oral product candidate from other small molecule, oral drugs. Small molecule based treatments for Gaucher disease, such as Zavesca and Eliglustat, have different and less specific mechanisms of action than those associated with ERT. We have filed patent applications with respect to this new protein delivery mechanism in countries with commercially significant markets. Currently, we are the exclusive owners of all rights to this technology.

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.

Oral GCD Development Program

We completed a phase I clinical trial of oral GCD in Israel for which we announced results in February 2014. It was an exploratory, open label study to evaluate the safety and pharmacokinetics of oral GCD in Gaucher patients. Patients receive re-suspended lyophilized carrot cells in a single oral administration during the first segment of the trial and three consecutive daily administrations during the second segment of the trial. The primary objective of the trial was to measure the safety of oral GCD in Gaucher patients. Additional objectives included an evaluation of oral GCD's pharmacokinetic profile and exploratory endpoints. The results demonstrate that oral GCD was well tolerated across all three doses tested. No patient discontinued the study prematurely, there were no drug related serious adverse events (SAE) reported and no treatment-induced antibodies were detected in any of the patients participating in the trial. All adverse reactions were transient in nature, mild and moderate and the patients that experienced the adverse reactions recovered without further events. One patient experienced nausea related to treatment and two patients experienced mild dizziness and dizziness, which was possibly related to treatment.

Pharmacokinetic (PK) studies revealed that active GCD enzyme was detected in the patients' blood circulation, measured in the well-established assay in leucocytes of Gaucher patients, following oral administration of oral GCD. C max analysis showed an average increase of over 100% in enzymatic activity from base line, with an increase ranging from approximately 50% to 350% among the different, individual patients in the study. In general, the PK profile of oral GCD has a pattern of continuous enzyme presence over approximately 30 hours from administration. Platelet levels in 3 out of 8 thrombocytopenic Gaucher patients tested showed meaningful, rapid and unexpected improvement in platelet count after short-term treatment with oral GCD. The data demonstrates platelet count increases ranging from 27% to 78% from base line. See Figure 4. Thus, with a daily oral administration of oral GCD, we expect to achieve a steady state level of active GCD enzyme in the blood circulation of patients similar to the physiological state in healthy individuals.

Figure 4. GCD Activity in Leukocytes Following Orally Delivered prGCD

Platelet levels in 3 out of 8 thrombocytopenic Gaucher patients tested showed meaningful, rapid and unexpected improvement in platelet count after short-term treatment with Oral GCD. The data demonstrates platelet count increases ranging from 27% to 78% from base line.

Preclinical studies of oral GCD were performed on rodents and large animals. To test the enzymatic activity of oral GCD, we tested the enzyme by feeding rats and pigs lyophilized carrot cells expressing GCD. The results of the study show that, based on preliminary PK data, we can detect the enzyme in the plasma of the animals, and that active enzyme is detected in the target organs, the spleen and liver, demonstrating the ability of a plant cell's cellulose wall to protect the enzyme against degradation in the animal's digestive tract. In addition, data from large and small animals demonstrate active absorbance of the protein in the plasma.

Figure 5. Pharmacokinetic profile of Oral GCD following oral administration, in pigs as compared to baseline sampling

Other Drug Candidates in Our Pipeline

We are developing other innovative recombinant therapeutic proteins to be expressed by our ProCellEx protein expression system, with an emphasis on treatments for which there are large, established pharmaceutical markets and where our proprietary protein expression system enables us to develop and commercialize recombinant proteins that are patent-protected and therapeutically equivalent or superior to the existing treatments. We select additional therapeutic candidates for development by testing candidates in-house and through collaborations with academic partners.

PRX-106; Oral antiTNF

Our oral antiTNF product candidate is a recombinant antiTNF (Tumor, Necrosis Factor) protein that we are expressing through ProCellEx. We are developing oral antiTNF an orally-administered treatment for immune mediated disorders using plant cells as a natural capsule for the expressed protein. In preclinical studies, oral PRX-106 alleviated immune-mediated hepatitis and reduced interferon gamma levels in a concanavalin A (ConA) inflammatory mouse model. Additionally, oral administration of PRX-106 alleviated immune mediated colitis in a well-established mouse model, promoting serum levels of anti-inflammatory IL-10 and regulatory T-cells. Oral antiTNF has an amino acid sequence that is similar to Enbrel which is one of the major treatments for patients of inflammatory diseases. Amgen Inc. reported total sales of Enbrel of approximately $4.6 billion, primarily in the United States, for 2013 and Pfizer has reported total sales of Enbrel outside of the United States and Canada of approximately $3.8 billion for 2013.

pr-antiTNF is a plant cell-expressed recombinant fusion protein made from the binding domain of the human TNF receptor (TNFR), fused to the Fc component of a human antibody domain. It has an identical amino acid sequence to Enbrel and our in vitro and preclinical animal studies have demonstrated that pr-antiTNF exhibits similar activity to Enbrel. Our earlier preclinical studies first focused on the intravenous administration of antiTNF. *In vitro* studies demonstrated that purified PRX-106 administered intravenously binds to TNF alpha, thereby inhibiting it from binding to cellular TNF receptors, and preventing its downstream effects, such as TNF-induced apoptosis, in a dose-dependent manner. In a proof-of-concept *in vivo* study using a well-established preclinical arthritis model, antiTNF (IV), when injected in mice, significantly improved clinical arthritis parameters, including joint inflammation, swelling and tissue degradation.

We are now conducting additional preclinical studies on oral antiTNF for several attractive indications, and we expect to initiate a phase I clinical trial of oral anti TNF for the oral treatment of autoimmune diseases in 2014.

PRX-110; DNase I

PRX-110 is our plant cell recombinant form of human deoxyribonuclease I (DNase I) that we are developing for the potential treatment of Cystic Fibrosis, to be administered by inhalation. DNase I cleaves extracellular DNA and thins the thick mucus that accumulates in the lungs of Cystic Fibrosis patients.

In vitro studies with PRX-110 demonstrated improved enzyme kinetics, less sensitivity to inhibition by actin and improved ex vivo efficacy when compared to Pulmozyme®, the only approved form of recombinant DNase I. Preclinical studies of PRX-110 administered by inhalation showed substantial enzymatic activity in lungs. We held a pre-IND meeting with the FDA in 2012 and plan to file an IND with the FDA in 2014.

Commercialization Agreement for taliglucerase alfa

On November 30, 2009, Protalix Ltd. and Pfizer entered into the Pfizer Agreement pursuant to which Pfizer was granted an exclusive, worldwide license to develop and commercialize taliglucerase alfa. Under the terms and conditions of the Pfizer Agreement, Protalix Ltd. retained the right to commercialize taliglucerase alfa in Israel and Brazil. In connection with the execution of the Pfizer Agreement, Pfizer made an upfront payment to Protalix Ltd. of $60.0 million in connection with the execution of the agreement and subsequently paid Protalix Ltd. an additional $5.0 million upon our filing of a proposed pediatric investigation plan to the Pediatric Committee of the EMA. Protalix Ltd. also received a milestone payment of $25.0 million in connection with the May 2012 approval of taliglucerase alfa by the FDA. In addition to the milestone payments, Protalix Ltd. is eligible to payments equal to 40% of the net profits earned by Pfizer on sales of taliglucerase alfa (or share 40% of the net loss). In calculating the net profits, there are certain agreed upon limits on the amounts that may be deducted from gross sales for certain expenses and costs of goods sold. Protalix Ltd. retained the manufacturing rights to taliglucerase alfa, and Pfizer and Protalix Ltd. agreed to a specific allocation of the responsibilities for the continued development efforts for taliglucerase alfa prior to its approval. Protalix Ltd. will manufacture all of the taliglucerase alfa needed for all purposes under the agreement and Pfizer will purchase the taliglucerase alfa from Protalix Ltd., subject to certain terms and conditions. The Pfizer Agreement also provides for reimbursement by Pfizer of certain costs to be incurred by Protalix Ltd.

In December 2012, we entered into a clinical development agreement with Pfizer pursuant to which Protalix will continue to manage, administer and sponsor current, ongoing clinical trials relating to taliglucerase alfa. Protalix is currently sponsoring adult and pediatric extension studies of taliglucerase alfa. New clinical trials for taliglucerase alfa will be conducted and sponsored by Pfizer. Protalix Ltd. received a milestone payment of $8.3 million upon the achievement of certain near-term clinical development milestones set forth in the agreement.

In connection with the upfront and milestone payments made under the Pfizer Agreement, Protalix Ltd. has paid a sublicense fee equal to $2.3 million to the academic institution from who it licensed certain technology relating to taliglucerase alfa. Any future regulatory approval milestone payment due under the Pfizer Agreement, if at all, will be subject to a 2.5% royalty, and all other revenues generated under the agreement will be subject to a 0.35% royalty payable to the same institution until 2016, when a patent related to taliglucerase alfa licensed to us will expire. We are also required to pay a royalty ranging between 3.0% and 6.0% of the revenues of taliglucerase alfa Pfizer records under the Pfizer Agreement to the Office of the Chief Scientist of Israel's Ministry of Industry, Trade and Labor, or the OCS.

We will be subject to a withholding tax on the U.S. revenue source portion of the payments made to us for our share of Pfizer's in net profits under the Pfizer Agreement. Currently, the withholding tax rate is 15%.

Technology Transfer Agreement with Fiocruz

We entered into the Brazil Agreement with Fiocruz in June 2013, which 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. Under the agreement, Fiocruz has committed to purchase at least approximately $40 million worth of taliglucerase alfa during the first two years of the term. In subsequent years, Fiocruz is required to purchase at least approximately $40 million worth of taliglucerase alfa per year. Additionally, we are not required to complete the final stage of the technology transfer until Fiocruz purchases at least approximately $280 million worth of taliglucerase alfa.

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.

To facilitate the arrangement with Fiocruz, we and Pfizer agreed to an amendment of our exclusive license and supply agreement, which amendment provides for the transfer of the commercialization and other rights to taliglucerase alfa in Brazil back to us. As consideration for the transfer of the commercialization and supply rights, we agreed to pay Pfizer a maximum amount of approximately $12.5 million from its net profits (as defined in the license and supply agreement) per year. Pfizer has also agreed to perform certain transitional services in Brazil on our behalf in connection with the supply of taliglucerase alfa to Fiocruz.

We will pay a fee equal to 5% of the net proceeds generated in Brazil to our agent for services provided in assisting us complete the Brazil Agreement pursuant to an agency agreement between us and the agent. The agency agreement will remain in effect with respect to the Brazil Agreement until the termination thereof.

Other Collaborations

Teva Pharmaceutical Industries

In September 2006, we entered into a Collaboration and Licensing Agreement with Teva for the development and manufacture of two proteins to be identified by Teva and us using our ProCellEx protein expression system. The agreement also identifies additional matters for collaboration between Teva and us. Subsequently, two proteins were identified to be researched and developed under the agreement but in 2009, both of the projects were terminated for commercial reasons. Pursuant to the agreement, we have agreed to collaborate on certain additional matters regarding proteins, including the research and development of proteins utilizing our ProCellEx protein expression system. See "Risk Factors—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."

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, 2013, we hold, or have license rights to 49 patents and 89 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. As of December 31, 2013, we hold, with a third party, one joint patent and one joint patent application, and licensed rights to five patents and six patent applications.

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.

As of December 31, 2013, our patent portfolio consists 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 have been issued, and hold licensed rights to, 19 patents in the United States, Australia, the European Union, Israel, Canada, the Czech Republic, Hungary, Japan, Poland, Mexico, Hong Kong, India and Korea, and to three pending patent applications. Among other things, the patents cover the methods that we use for culturing and harvesting plant cells and/or tissues in consecutive cycles. Of the issued patents in this family, 13 are expected to expire in 2017 and six are expected to expire in 2025.

- With respect to our ProCellEx protein expression system, we hold two issued patents and 14 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 are expected to expire in 2028.

- We hold a patent family containing 16 granted patents in India, South Africa, Russia, Australia, China, the United States, Ukraine, Singapore, Japan, Europe, Hong Kong, Mexico and Korea, and 20 patent applications relating to the production of recombinant glycosylated lysosomal proteins in our plant culture platform, including taliglucerase alfa, and uses of these proteins and of 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 are expected to expire in 2024.

- We hold a patent family containing four 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 patents to issue in the future based on the patent applications in this patent family are expected to expire in 2025.

- We hold a patent family containing three issued patents in South Africa, Australia and Singapore, and 13 pending patent applications 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 are expected to expire in 2026.

- We hold a patent family containing two granted patents in South Africa and Australia, and five pending patent applications relating to saccharide containing protein conjugates. The patents to issue in the future based on the patent applications in this patent family will expire in 2028.

- We hold a patent family containing 10 pending patent application 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 will expire in 2031.

- We hold a patent family containing 14 pending patent applications and one granted patent relating to multimeric protein structures of -galactosidase and to uses thereof in treating Fabry disease. The patents to issue in the future based on the patent applications in this patent family are expected to expire in 2031.

- We hold a patent family containing three pending patent applications relating to therapeutic proteins with stabilized quaternary structure. The patents to issue in the future based on the patent applications in this patent family will expire in 2031.

- We hold a patent family containing one granted patent in Europe and two pending patent applications relating to multimeric protein structures of glucocerebrosidase and to uses thereof in treating Gaucher disease. The patents to issue in the future based on the patent applications in this patent family will expire in 2031.

- We hold three patent families containing three PCT applications relating to plant recombinant human DNase I and uses in therapy. The patents to issue in the future based on these patent applications are expected to expire in 2033.

- We hold patent applications relating to plant recombinant TNF alpha inhibitor polypeptides.

- 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.

- With respect to taliglucerase alfa, we have licensed the rights to two patents from Virginia Tech Intellectual Properties, Inc., or Virginia Tech, that are expected to expire in 2016.

- We co-own a patent application that covers use of plant cells expressing a TNF alpha polypeptide inhibitor in therapy.

- We hold one patent family relating to Oral delivery of plant cells comprising recombinant glucocerebrosidase for the treatment of Gaucher disease. The patents to issue in the future based on patent application in this patent family are expected to expire in 2034.

- We hold a patent application relating to plant recombinant human alpha 1 anti-trypsin.

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. Under the terms of the agreement, 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.

In January 2005, Protalix Ltd. entered into a license agreement with Virginia Tech University, pursuant to which we received a non-exclusive worldwide license to make, have made, use, sell, offer for sale and import certain of Virginia Tech’s patents. As consideration for the license, we made a one-time license fee payment to Virginia Tech, and we are obligated to make royalty payments equal to varying low, single-digit percentages of net sales of licensed products by Protalix Ltd., its subsidiaries and/or their affiliates. Upon commercialization of a licensed product, the royalty payment is subject to a low, annual minimum amount. In addition, we were obligated to make milestone payments equal to $150,000, in the aggregate, upon the achievement of certain milestones, which milestone payments have been satisfied. We have the right to grant sublicenses under the agreement.

Our license agreement with Virginia Tech remains in effect until the earlier of the expiration of the last patent under the agreement or 10 years after the first commercial sale of any licensed product. Virginia Tech may terminate the agreement upon written notice to us that we are in material breach of our obligations under the agreement if we are unable to remedy such material breach within a fixed number of days after we receive such notice, which number may be doubled if we are making good faith efforts to achieve a cure and the extension will not increase the damages suffered by Virginia Tech. We have the right to terminate the agreement at any time upon prior written notice delivered an agreed-upon number of days prior to the date of termination.

Manufacturing

We are obligated to manufacture all of the taliglucerase alfa drug product needed under the Pfizer Agreement, subject to certain terms and conditions. Our drug product candidates, including 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 use our current facility, which has approximately 20,000 sq/ft of clean rooms built according to industry standards, to develop, process and manufacture taliglucerase alfa and other recombinant proteins. We intend to use our current manufacturing space to produce all of the taliglucerase alfa we need in the near future, included the taliglucerase alfa to be purchased by Pfizer. In addition, we intend to use our manufacturing space to produce all of the drug substance needed in connection with the clinical trials of PRX-102 and of our oral treatment of Gaucher disease, and potentially for our other product candidates. Current capacity of our facility can serve all of our current and expected commercial and clinical needs.

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.

We have engaged a contract manufacturer in Europe to act as an additional source of fill and finish activities for taliglucerase alfa. According to our agreement with Pfizer, Pfizer will be responsible for the fill and finish activities for taliglucerase alfa. We have engaged other contract manufacturers to perform fill/finish activities for PRX-102 and for our oral treatment of Gaucher disease.

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 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 our 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.

We specifically face competition from companies with approved treatments of Gaucher disease. In addition to ELELYSO, there are two other ERTs for the treatment of Gaucher disease; Cerezyme which is marketed by Genzyme (acquired by Sanofi) and VPRIV, which is marketed by Shire. To a much lesser extent, we also compete with Actelion. In addition, Genzyme is developing Eliglustat which is in the late stages of clinical development and was the subject of a phase III clinical trial that was completed in 2013. Eliglustat is a small molecule, oral drug which is being developed for the treatment of Gaucher disease.

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. In 2012, Shire withdrew its BLA for Replagal in the United States. In addition, we are aware of other clinical stage, early clinical stage and experimental drugs which are being developed for the treatment of Fabry disease by Amicus Therapeutics and other companies.

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, and Greenovation Biotech GmbH, none of which are cell-based. Rather, such companies base their product development on transgenic plants or whole plants.

Several biogeneric companies are pursuing the opportunity to develop and commercialize follow-on versions of other currently marketed biologic products, including growth factors, hormones, enzymes, cytokines and monoclonal antibodies, which are areas that interest us. These companies include, among others, Novartis AG/Sandoz Pharmaceuticals, BioGeneriX AG, Stada Arzneimittel AG, BioPartners GmbH and Teva. 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

Members of our scientific advisory board, who are experts in the fields of plant molecular and cell biology as well as Gaucher disease and various hematological and genetic disorders, 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	Affiliation
	Laureate of the Nobel Prize in Chemistry
	Member, U.S. National Academy of Sciences
Roger D. Kornberg, Ph.D.	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)
	Laureate of the Nobel Prize in Chemistry
Professor Aaron Ciechanover, M.D., D.Sc.	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
Professor Gad Galili, Ph.D.	Former Chairman of the Department of Plant Sciences, The Weizmann Institute of Science, Rehovot, Israel
	Director of the Gaucher Clinic, Shaare Zedek Medical Center, Jerusalem, Israel
Professor Ari Zimran, M.D.	Associate Professor of Medicine, Hebrew University-Hadassah Medical School, Jerusalem, Israel

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, an NDA is submitted to the FDA for its 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. In September 2009, we received orphan drug designation for taliglucerase alfa for the treatment of Gaucher disease. 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, FDA may grant orphan drug approval and provide a seven-year period of marketing exclusivity.

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. For a fast track product, the FDA may consider for review on a rolling basis sections of the NDA before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA as they become available and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. We used the rolling submission 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 (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 rate.

On July 14, 2009 the Economic Efficiency Law (Legislation Amendments for the Implementation of the Economic Plan for the years 2009 and 2010), 2009, or the 2009 Amendment, was passed in the Knesset; this law determined, inter alia, a further gradual reduction of the corporate tax rate as from 2011, as follows: 2011 – 24%, 2012 – 23%, 2013 – 22%, 2014 – 21%, 2015 – 20%, 2016 and thereafter – 18%.

On December 6, 2011, the “Tax Burden Distribution Law” was officially published, discontinuing a previously approved gradual decrease in corporate tax provided in the 2009 Amendment, and setting the corporate tax rate in Israel for 2012 and thereafter to 25%.

On August 5, 2013, the Law for Change of National Priorities (Legislative Amendments for Achieving the Budgetary Goals for 2013-2014), 2013 was published in Reshumot (the Israeli government official gazette), enacting, among other things, an increase in the corporate tax rate beginning in 2014 and thereafter to 26.5% (instead of 25%).

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

In addition to the corporate taxes in Israel, we are subject to a withholding tax on the U.S. revenue source portion of the payments made to us for our share of Pfizer's net profits under the Pfizer Agreement. The withholding tax rate is 15%. See "Business—Commercialization Agreement."

Law for the Encouragement of Capital Investments, 1959.

The Law for the Encouragement of Capital Investments, 1959, 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 "Investment Center" of the Israeli Ministry of Industry, Trade and Labor, or the Investment Center. 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 Investment Center 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 and Development Law, 1984

To date, Protalix Ltd. has received grants from the OCS for the financing of a portion of its research and development expenditures in Israel. As of December 31, 2013, the OCS approved grants in respect of Protalix Ltd.'s continuing operations totaling approximately $31.8 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 the OCS through payments of royalties at a rate of 3% to 6% of the revenues generated from an OCS-funded project, depending on the period in which revenues were generated. As of December 31, 2013, Protalix Ltd. either paid or accrued royalties payable of $4.7 million and Protalix Ltd.'s contingent liability to the OCS with respect to grants received was approximately $27.6 million.

Under the Israeli Law for the Encouragement of Industrial Research and Development, 1984, and related regulations, or the Research Law, recipients of grants from the OCS 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 the OCS-financed technologies and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the approval of the OCS' Research Committee. Protalix Ltd. may not receive the required approvals for any proposed transfer and, if received, Protalix Ltd. may be required to pay the OCS 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 the OCS, the amount of time that has elapsed between the date on which the know-how was transferred and the date on which the OCS 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 the OCS. 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, the Research Committee to allow the transfer outside of Israel of know-how derived from an approved program and the related manufacturing rights. In general, the Research Committee may approve transfer of know-how in limited circumstances 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 the OCS an amount, in cash, as set forth in the Research Law. 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 the OCS as set forth in the Research Law.

- 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 the OCS 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 OCS funding and there is no restriction on the export of products manufactured using technology developed with OCS 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.” OCS 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 & Samara 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 developme