PROTALIX BIOOTHERAPEUTICS, INC.

FORM 8-K
(Current report filing)

Filed 01/05/18 for the Period Ending 01/05/18

Telephone 972-4-988-9488
CIK 0001006281
Symbol PLX
SIC Code 2836 - Biological Products, (No Diagnostic Substances)
Industry Biotechnology & Medical Research
Sector Healthcare
Fiscal Year 12/31
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of
the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event
Reported): January 5, 2018

Protalix BioTherapeutics, Inc.
(Exact name of registrant as specified
in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-33357
(Commission File Number)

65-0643773
(IRS Employer
Identification No.)

2 Snunit Street
Science Park, POB 455
Carmiel, Israel
(Address of principal executive offices)

 Registrant’s telephone number, including area code +972-4-988-9488

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions ( see General Instruction A.2. below):

☐ Written communication pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communication pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communication pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐
Item 2.02. Results of Operations and Financial Condition

On January 5, 2018, Protalix BioTherapeutics, Inc. (the “Company”) released its January 2018 Corporate Update. A copy of the update will be posted in the Presentations page of the Investors tab of the Company’s corporate website and is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

All of the information furnished in Item 2.02 and Exhibit 99.1 shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liability of that section, and shall not be incorporated by reference into any registration statement or other document filed under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

99.1 January 2018 Corporate Update.
SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 5, 2018

PROTALIX BIOTHERAPEUTICS, INC.

By: /s/ Moshe Manor
Name: Moshe Manor
Title: President and
Chief Executive Officer
Note Regarding Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The forward-looking statements included, among others, statements regarding expectations as to regulatory approvals, market opportunity for, and potential sales of, the Company’s product and product candidates, goals as to product candidate development and timing of the Company’s clinical trials, are based on the Company’s current intent, belief and expectations. These statements are not guarantees of future performance and are subject to certain risks and uncertainties that are difficult to predict. Factors that might cause material differences include, among others: failure or delay in the commencement or completion of the Company’s preclinical and clinical trials which may be caused by several factors, including: slower than expected rates of patient recruitment; unforeseen safety issues; determination of dosing issues; lack of effectiveness during clinical trials; inability to monitor patients adequately during or after treatment; inability or unwillingness of medical investigators and institutional review boards to follow the Company’s clinical protocol; and lack of sufficient funding to finance clinical trials; the risk that the results of the clinical trials of the Company’s product candidates will not support the Company’s claims of safety or efficacy, that the Company’s product candidates will not have the desired effects or will be associated with undesirable side effects or other unexpected characteristics, the Company’s dependence on performance by third party providers of services and supplies, including without limitation, clinical trial services; delays in the Company’s preparation and filing of applications for regulatory approval; delays in the approval or potential rejection of any applications we file with the FDA or other health regulatory authorities, and other risks relating to the review process; the inherent risks and uncertainties in developing drug platforms and products of the type we are developing; the impact of development of competing therapies and/or technologies by other companies and institutions; potential product liability risks, and risks of securing adequate levels of product liability and other necessary insurance coverage, and other factors described in the Company’s filings with the U.S. Securities and Exchange Commission. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of today’s date. The Company undertakes no obligation to update or revise the information contained in this presentation whether as a result of new information, future events or circumstances or otherwise.
Company Highlights

➢ FDA approved ProCellEx® plant cell-based expression system being utilized to develop clinically differentiated and improved recombinant therapeutic proteins. FDA multi-product and EMA approved manufacturing facility in Carmiel, Israel.

➢ Pegunigalsidase alfa in Phase III for Fabry disease >$1.2B growing market; potential to be best-in-class with a superiority claim:
  • Ex US exclusive license to Chiesi Farmaceutici S.p.A. – $50M in payments prior to results
  • Orphan Drug Designation (ODD) granted in EU

➢ Two Phase II candidates with business development opportunities
  • Inhaled alidornase alfa for Cystic Fibrosis targeting an ~ $700M market with growth potential
  • Oral anti-TNF alpha for inflammatory bowel diseases targeting >$5B market

➢ Eleyso® (alfataliglucerase) approved and commercialized for Gaucher disease – Protalix retains rights in Brazil; $24M order secured
Corporate Strategy

**Execution** of Phase III Fabry clinical trial program and key data read-outs and potential global approvals

**Focus on additional partnering** opportunities for assets in development

**Generate revenue** through sales of alfataliglucerase in Brazil

**Advancement** of early pipeline products into clinical development
Pipeline Overview

- Pegunigalsidase alfa (PRX 102) - Fabry Disease
- Alidornase alfa (PRX 110) - Cystic Fibrosis
- Oral anti-TNF (OPRX-106) - Ulcerative Colitis/Inflammatory diseases
for Fabry Disease
Fabry disease remains a high unmet need

- Rare genetic lysosomal storage disorder caused by deficiency in the enzyme α-galactosidase A. Lipids accumulate in key organs (kidney, heart, CNS) leading to a progressive and potentially life threatening disease.

- “Little functional enzyme every second week and presence of anti-agalsidase antibodies are likely contributors to the limited effect of ERT”*

- High treatment burden and challenging compliance with bi-weekly infusions

- >$1.2B growing market (CAGR ~10%) ~5,000 patients treated worldwide.

<table>
<thead>
<tr>
<th>Key Players</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Fabrazyme®, Sanofi</td>
<td>Enzyme Replacement Therapy (ERT) &amp; bi-weekly infusions</td>
<td>Approved Worldwide</td>
</tr>
<tr>
<td>Replagal®, Shire</td>
<td></td>
<td>Approved ex-US only</td>
</tr>
<tr>
<td>Galafold™, Amicus</td>
<td>pharmacological chaperone</td>
<td>Approved in EU only &amp; Only for patients with amenable mutations (~30%)</td>
</tr>
</tbody>
</table>

*Consensus by key opinion leaders experts in Fabry disease, April 2017
Unique proposition for addressing significant unmet needs

- A chemically modified plant cell derived PEGylated enzyme. Designed to be superior to the currently approved ERTs
- Two dosing regimens: potential for better efficacy and lower treatment burden

<table>
<thead>
<tr>
<th>1mg/kg/2weeks</th>
<th>2mg/kg/4weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Superior</strong> ERT for patients with progressing impaired renal function</td>
<td><strong>Better</strong> quality of life by maintaining clinical stability with 50% less infusions</td>
</tr>
</tbody>
</table>

- Treatment flexibility for patients
- Two independent paths for product superiority
Substantially greater enzyme exposure than current ERTs

Higher levels of active available enzyme → potentially more efficacious

* Fabrazyme® (agalsidase beta) – USPI

[Graph showing comparison of enzyme levels and half-lives between pegunigalsidase alfa and Fabrazyme®]
PK modeling shows greater AUC in a single infusion of 2 mg/kg pegunigalsidase alfa vs. two bi-weekly infusions of Fabrazyme® over a 4 week time frame.
Phase I/II – 24 month data

Positive impact on kidney function

<table>
<thead>
<tr>
<th>Pegunigalsidase alfa (eGFR BL 82.4-156.3)</th>
<th>Fabrazyme® (eGFR BL 49-170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR slope(^1)</td>
<td>-2.2*</td>
</tr>
<tr>
<td></td>
<td>-3.8</td>
</tr>
</tbody>
</table>

* N=7 classic Fabry patients

Excellent safety and tolerability profile

- Favorable safety and tolerability observed throughout ~35 patient years
- 19% formation of anti-drug antibodies (ADAs) in pegunigalsidase alfa vs. 74% with Fabrazyme®
- All ADA positive patients turned negative in the second year following treatment, leaving 0% of present anti-drug antibodies
- Any ADA positivity with pegunigalsidase alfa had no observed impact on safety and efficacy

1. Measured as Annualized Rate of Estimated GFR Change (mL/min/1.73 m\(^2\)/year) – 24 months
2. Germain et al 2015
Continuous reductions observed over 24 months

Plasma Gb3 and Lyso-Gb3

Gastrointestinal symptoms

n=11
Continuous clinical stability observed over 24 months

Stable Renal Function

Stable Cardiac Parameters (by MRI)
Mean LVM, LVMI and EF
Clinical advantage recognized with granting of EU Orphan Drug Designation (ODD)

Although other therapies for Fabry Disease are approved for use in the EU, the European Commission granted Orphan Drug Designation (ODD) for pegunigalsidase alfa for the treatment of Fabry disease based on:

- Pegunigalsidase alfa demonstrated **clinically relevant advantages over authorized therapies:**
  - Reduced peripheral neuropathy
  - Reduced immunogenicity

- In addition to these advantages pegunigalsidase alfa has demonstrated significant benefit:
  - Reduced accumulation of toxic metabolites in relevant tissues
  - Clinical data demonstrating the stabilization of kidney function
Ex US exclusive collaboration with Chiesi Farmaceutici S.p.A.

- Chiesi, an international privately-held company, strong presence outside US, with focus on the development and commercialization of innovative medicines

- In exchange for ex-US commercialization rights for pegunigalsidase alfa:
  - Upfront payment of $25 million and additional payments of up to $25 million in development costs
  - Eligibility for an aggregate of $320 million in regulatory and commercial milestones as well as tiered royalties ranging from 15% to 35%

- Protalix remains the manufacturer for clinical development and commercial product.
  - Validates Protalix’s Fabry program
  - Secures funding for clinical program
  - A focused and effective commercialization partner
  - Protalix maintains US rights
Robust Phase III pivotal clinical program

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<thead>
<tr>
<th></th>
<th>balance</th>
<th>bright</th>
<th>bridge</th>
</tr>
</thead>
<tbody>
<tr>
<td>1mg/kg 2 weeks</td>
<td>Head to Head vs. Fabrazyme® in Switch Patients</td>
<td>2mg/kg 4 weeks Switch-over from Fabrazyme® and Replagal®</td>
<td>1mg/kg 2 weeks Switch-over from Replagal®</td>
</tr>
<tr>
<td>FDA</td>
<td>24 mos Superiority</td>
<td>12 mos Safety and efficacy</td>
<td>12 mos Supportive</td>
</tr>
<tr>
<td>EMA Rest of World</td>
<td>12 mos Comparability (potential for superiority)</td>
<td>12 mos Safety and efficacy</td>
<td>12 mos Safety and efficacy</td>
</tr>
<tr>
<td>Number of patients</td>
<td>78 (52+26)</td>
<td>30</td>
<td>22</td>
</tr>
</tbody>
</table>
Potential to be gold standard therapy

Peak Sales Potential over $1B Annually (>50% market share)

1 mg/kg / 2 weeks
Potential superiority in efficacy

<table>
<thead>
<tr>
<th></th>
<th>Fabrazyme</th>
<th>pegunigalsidase alfa</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR slope</td>
<td>-3.8</td>
<td>-2.2*</td>
</tr>
<tr>
<td>Half life</td>
<td>2 hours</td>
<td>~80 hours</td>
</tr>
<tr>
<td>Active enzyme</td>
<td>½ day</td>
<td>&gt;14 days</td>
</tr>
<tr>
<td>Antibody presence</td>
<td>74%</td>
<td>0%**</td>
</tr>
</tbody>
</table>

Once monthly 2 mg/kg
50% less infusions

- One month of active enzyme
- Clinical efficacy maintained
- Enhanced quality of life
- Lower treatment burden

*N=7 classic Fabry patients, 24 months
**15% formation of anti-drug antibodies (ADAs)/ All ADAs turned negative in the second year following treatment, leaving 0% of present anti-drug antibodies
alidornase alfa (PRX-110) for Cystic Fibrosis
Cystic Fibrosis (CF) is a rare genetic disease characterized by a highly viscous mucus most prominently leading to severe lung damage and loss of respiratory function. Over 70,000 CF patients worldwide.

Leading product, Pulmozyme®, DNase enzyme, ~$700M annual sales with significant growth potential.

Alidornase alfa (PRX 110) was designed as a recombinant DNase resistant to actin inhibition to enhance enzyme activity.

In human sputa samples, alidornase alfa exhibits superior activity compared to Pulmozyme® in breaking down extracellular DNA and lowering sputum viscosity which translates to potentially improving lung function.

Can potentially lower incidence of respiratory tract infections.
Phase II trial demonstrates clinically meaningful lung function improvement

Mean absolute change in ppFEV1

<table>
<thead>
<tr>
<th>Absolute change in ppFEV1 (Mean ± SE)</th>
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<tbody>
<tr>
<td>baseline vs. Pulmozyme</td>
</tr>
<tr>
<td>alidornase alfa vs. Pulmozyme®</td>
</tr>
<tr>
<td>alidornase alfa vs. Baseline</td>
</tr>
<tr>
<td>Follow up vs. alidornase alfa</td>
</tr>
</tbody>
</table>

N=16
Clinically meaningful lung function improvement as a result of effective mucociliary clearance

Extraordinary reduction of the presence of Pseudomonas aeruginosa (P. sa) infections as a result of alidornase alfa treatment - All P. sa positive patients showed an >75% reduction of which 60% experienced total eradication.

- potential for lowering respiratory tract infections
- potential for reduction in CF exacerbations

Safe, tolerable and shorter inhalation time

Cystic Fibrosis Foundation approves letter of application enabling Protalix to apply for grant funding

Based on the positive results in phase II, a medical advisory board has been assembled consisting of 12 leading KOLs across the globe to determine upcoming development plan
Oral anti-TNF
OPRX-106
for Ulcerative Colitis
With Protalix’ platform for orally delivered proteins, the plant cell wall protects the protein and serves as a natural oral administration vehicle.

OPRX 106 is a plant cell-expressed recombinant anti-TNF fusion protein.

Anti-TNF market >$30B with multiple blockbuster products all of which are injections and IV infusions.

Multiple indications:

- Ulcerative colitis (~$5.5B)
- Rheumatoid arthritis (~$17B)
- Psoriasis (~$5.7B)
- Crohn’s disease (~$3.6B)
OPRX 106  
Clinical Program for Ulcerative Colitis

Phase I – 15 Healthy Volunteers - COMPLETED

- Safe and well tolerated.
- Alteration of systemic immune system with no systemic absorption

Phase II – ONGOING

- Enrollment completed – 24 mild to moderate ulcerative colitis patients
- First 14 patients completed the study and four patients still ongoing
- Oral once daily administration - 8 week follow-up
- Evaluating two doses for:
  - Efficacy parameters: Mayo score, rectal bleeding, fecal calprotectin level
  - Safety and tolerability
  - Pharmacokinetics
- Complete results expected by end of Q1 2018
Positive interim results of 14 patients: Improvement for majority of patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Response(^1)</td>
<td>8/14 57%</td>
</tr>
<tr>
<td>Clinical Remission(^2)</td>
<td>5/14 36%</td>
</tr>
<tr>
<td>Improved rectal bleeding score (^3)</td>
<td>11/14 79%</td>
</tr>
<tr>
<td>Fecal calprotectin</td>
<td>12/14 86%</td>
</tr>
<tr>
<td>Geboes score</td>
<td>9/14 64%</td>
</tr>
</tbody>
</table>

1. Clinical response: Reduced Mayo score >3 points and decrease in the rectal bleeding sub-score of >1 point from baseline, or a rectal bleeding sub-score of 0 or 1
2. Clinical remission: Mayo score of ≤ 2 with no sub-score reaching >1 point
3. Rectal bleeding sub-score = 0 or 1 point

- OPRX 106 was safe and well-tolerated. Adverse events (AEs) were mild to moderate and transient with headaches the most common adverse event
- No immunosuppression was evident
Financial Overview

- ~144M shares outstanding, as of December 31, 2017
- Dual listed on NYSE MKT and TASE
- Cash position: ~$50.5M as of December 31, 2017
- Cash level currently projected to fund operations into 2020
- $5.9M convertible note due by September 2018, ~$59M convertible note due by November 2021
- 10 years of 0% tax after using up NOL (currently ~$150M)
Protalix has an exciting road ahead...

- Two year data for pegunigalsidase alfa
- Promising results for alidornase alfa and OPRX 106
- Clinical development pipeline targeting markets ~$7B
- R&D focus to advance early pipeline with attractive opportunities for proteins designed for superior clinical profiles

And multiple near term catalysts in the next 12 months

1. Report final results from Phase II for oral anti-TNF (OPRX-106)
2. Finalize enrollment in Phase III pegunigalsidase alfa studies
3. Continue partnership transactions
4. Introduce new pipeline (currently in preclinical)
Thank You

Moshe Manor
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