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Protalix BioTherapeutics, Inc. (PLX - NYSE)

$40 Million Raise; SarcoMed Licensing

Based on our DCF model and a 15% discount rate, Protalix is valued at approximately $15.00 per share. Our model applies an 85% probability of ultimate approval and commercialization for PRX-102 in Fabry Disease. The model includes contributions from a global commercialization effort.

Current Price (2/17/21)	$4.74
Valuation	**$15.00**

OUTLOOK

Protalix is a clinical and commercial pharmaceutical company using its proprietary ProCellEx plant-based expression system to produce therapeutic proteins for global markets. The company has one commercialized product, Elelyso that is marketed by Fiocruz in Brazil & Pfizer in the rest of the world for Gaucher Disease. Other candidates include PRX-102 for Fabry Disease, now under review by the FDA with an anticipated target action date of April 27, 2021. If approved, Chiesi Rare Disease will commercialize the product globally.

Protalix has additional candidates in earlier stages of development including OPRX-106 for IBD and PRX-110 for Cystic Fibrosis. The company also has a partnership with SarcoMed for development of PRX-110 in Pulmonary Sarcoidosis.

We expect PRX-102 to be approved and sales related payments to be received in 2021. PRX-102 can fill an unmet need with several improvements over the market leader and is expected to command a premium to existing products. Elelyso is expected to show moderate growth over the next quarters as partners continue their commercialization efforts. Profits from revenue generating products are expected to be invested in new candidates in coming years.

SUMMARY DATA

52-Week High	**$7.02**
52-Week Low	**$2.04**
One-Year Return (%)	**32.4**
Beta	**2.83**
Average Daily Volume (sh)	**455,691**
Shares Outstanding (mil)	**33.3**
Market Capitalization ($mil)	**158**
Short Interest Ratio (days)	**2.0**
Institutional Ownership (%)	**15.9**
Insider Ownership (%)	**32.8**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**2.0**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2020 Estimate	**N/A**
P/E using 2021 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in millions of US$)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	$10.4 A	$12.2 A	$14.2 A	$17.8 A	$54.7 A
2020	$21.6 A	$11.0 A	$10.8 A	$10.6 E	$53.8 E
2021					$48.9 E
2022					$78.4 E

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$0.49 A	-$0.52 A	-$0.24 A	$0.02 A	-$1.23 A
2020	$0.10 A	-$0.13 A	-$0.14 A	-$0.13 E	-$0.39 E
2021					-$0.01 E
2022					$1.06 E

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WHAT'S NEW

Since Our Initiation

Over the last few weeks, Protalix Biotherapeutics, Inc. (NYSE: PLX) has posted several updates including the announcement of pricing and closing of its latest, ~$40 million financing. The company has also consummated an exclusive partnership with SarcoMed USA, presented BRIDGE data at the 17th Annual WORLDSymposium, issued a Letter to Shareholders and announced final results from the BRIDGE trial. We see the most important event as the successful closing of the financing which removes the refinancing overhang related to the repayment of the $57.9 million of convertible notes that are due in November 2021.

Public Offering

On February 11, 2021, Protalix both proposed a public offering of common stock and announced its pricing. The company planned to issue 7,608,695 shares at $4.60 per share with a 15% over-allotment option for up to 1,141,304 additional shares. Bank of America Securities acted as the book-running manager and Oppenheimer & Co. as the co-manager for the offering. Net proceeds will be used to fund clinical trials for Protalix candidates and R&D activities and for working capital for general corporate purposes. The completion of the raise was announced February 18, 2021, with gross proceeds totaling approximately $40.25 million and the overallotment exercised in full.

Exclusive Partnership with SarcoMed USA

Protalix announced on February 11 that it had entered into an exclusive partnership with SarcoMed USA to develop alidornase alfa for the treatment of pulmonary sarcoidosis. This is the culmination of a July 2020 non-binding term sheet between the two companies. SarcoMed USA is a private company that was formed in 2017 to support its lead product candidate, SM001, a recombinant DNase I delivered via inhalation, in pulmonary sarcoidosis. The agreement grants exclusive worldwide license for alidornase alfa (PRX-110), Protalix' Phase II recombinant DNase I, for use in the treatment of any human respiratory disease including, but not limited to, sarcoidosis, pulmonary fibrosis and other related diseases via inhaled delivery.

Under the terms of the agreement, SarcoMed will be responsible for identifying, selecting and conducting clinical research and development of pharmaceutical candidates. In return for the license, Protalix is entitled to upfronts of $3.5 million, subject to conditions, additional payments tied to regulatory and commercial milestones and tiered royalties on product net sales commercialized through the license. Clinical and commercial supply agreements are agreed to enter talks within the next 60 days, else SarcoMed can terminate the license agreement.

PRX-110

Alidornase alfa is recombinant human deoxyribonuclease I (DNase I) expressed via the ProCellEx platform. Administration is via inhalation for direct application to the lungs. DNase I therapy can act as a mucus thinning agent (mucolytic) to help with clearance from the airways to improve lung function and reduce the chances of infection. Disintegrating inflammatory cells, namely neutrophils, release DNA into the sputum, which polymerizes and is present at high concentrations, contributing to the viscosity of the sputum. DNase I degrades the DNA, thus reducing the viscosity of the mucus.[1]

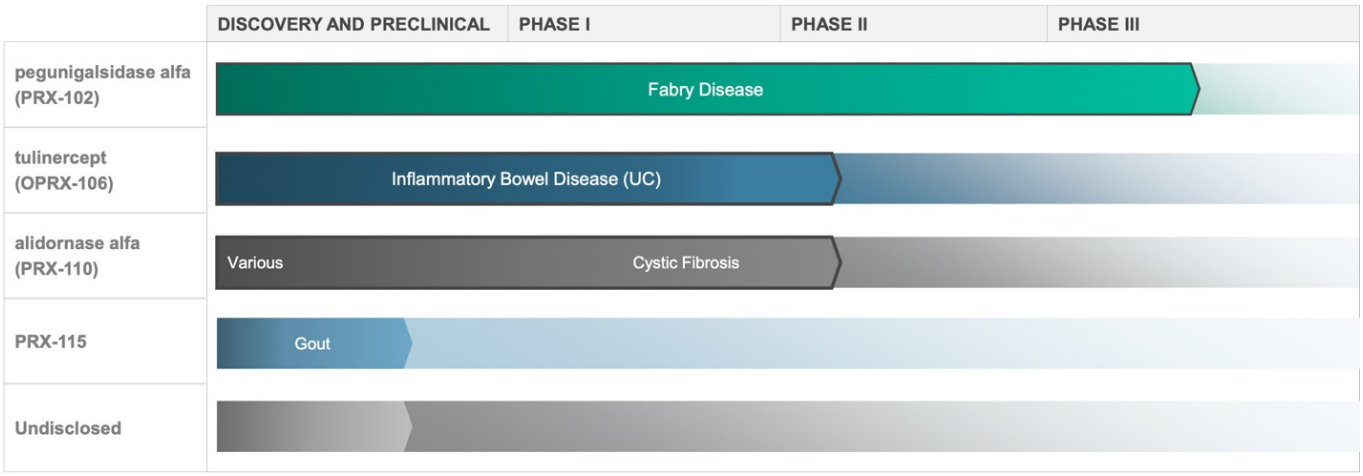
BRIDGE Phase III Final Results

On December 30, 2020, Protalix announced final results of its BRIDGE Phase III open-label, switch-over clinical trial of lead candidate pegunigalsidase alfa (PRX-102) in Fabry Disease.

Protalix uses a plant-based protein expression system, ProCellEx, to produce its biologics. In 2012, Protalix successfully gained FDA approval for Elelyso making it the first FDA approved biologic expressed with a plant-based system. While Elelyso is already approved, Protalix has additional, clinical-stage candidates including PRX-102 which is under review by the FDA with a target action date of April 27, 2021.

[1] Pressler T. (2008). Review of recombinant human deoxyribonuclease (rhDNase) in the management of patients with cystic fibrosis. *Biologics: targets & therapy*, *2*(4), 611–617. https://doi.org/10.2147/btt.s3052

Protalix Clinical Development Pipeline[2]



PRX–102 is a recombinant α-Galactosidase-A enzyme. Protalix uses its ProCellEx platform to express the enzyme and then chemically modifies it via surface pegylation. Protein sub-units are covalently bound via chemical cross-linking using short PEG moieties, resulting in a molecule with unique pharmacokinetic parameters. In clinical studies, PRX–102 has demonstrated a circulatory half-life of approximately 80 hours. Due to the chronic nature of Fabry, patients must receive IV infusion of enzyme replacement therapy every two weeks, which is a significant burden. PRX-102, with its extended half-life, aims not only to be more effective, but also reduce the frequency of doctors' visits by Fabry patients.

Three Phase III studies were launched to support regulatory approval of PRX-102 around the globe, designated BRIDGE, BALANCE and BRIGHT. After a release of topline results in May 2020, the BRIDGE trial provided final results on December 30, reiterating its findings of a substantial improvement in renal function.

BRIDGE was a 12-month open-label, single arm switch-over study evaluating the efficacy of 1 mg/kg of pegunigalsidase alfa infused every two weeks. The 22 Fabry patients in the trial had been previously treated with agalsidase alfa (Replagal) for at least two years and had been stable on this drug for at least six months.

BRIDGE Final Results

The study found a mean annualized estimated glomerular filtration rate (eGFR) slope of the study participants improvement from -5.90 mL/min/1.73m^2/year while on agalsidase alfa to -1.19 mL/min/1.73m^2/year on PRX-102 in all patients. Male patients improved from -6.36 mL/min/1.73m^2/year to -1.73 mL/min/1.73m^2/year and female patients improved from -5.03 mL/min/1.73m^2/year to -0.21 mL/min/1.73m^2/year.

Baseline characteristics of the 20 completed patients, ranging from ages 28 to 60 years, were as follows: mean eGFR 75.87 in males and 86.14 in females and plasma lyso-GL-3[3] mean levels were 51.8 nM and 13.8 nM in males and females, respectively. While lyso-GL-3 levels remained somewhat high, particularly within the male cohort, continuous reduction in lyso-GL-3 levels was observed of 19.55 nM (32.35%) in males and 4.57 nM (29.81%) in females. Lyso-GL-3 is a biomarker that indicates the status of the patient and whether or not they are improving but is not related to a patient's clinical symptoms.

The shift to PRX-102 resulted in a decrease of kidney disease progression and most patients were stable after the change. PRX-102 was well tolerated during the study. All adverse events were transient without sequelae. Of the 22 patients enrolled, the majority of treatment emergent adverse events (TEAE) were mild or moderate. Two patients (9.1%) withdrew from therapy due to hypersensitivity reaction that resolved. The most common TEAEs were nasopharyngitis, headache and dyspnea.

The final results provided an immunogenic analysis, adding to the details reported in May. Over the duration of the study, patient serum was collected at monthly frequency and screened for the presence and amount of immunoglobulin (antibodies) that were active against PRX-102. An immunogenicity assessment indicated that 4 out of 20 patients (20%) developed persisting antidrug antibodies over the study period, two of which had antibodies with

[2] Protalix Corporate Presentation September 2020
[3] Lyso-GL-3, also referred to as Lyso-Gb3, is a biomarker with limited correlation to symptoms, but is highly sensitive as a therapeutic monitor.

neutralizing activity.[4] However, two of the four patients were positive at baseline following treatment with Replagal, suggesting pre-existing antibodies that were cross-reactive with PRX-102. Furthermore, based on statistical analysis, efficacy and safety were unaffected by whether the patient was antibody positive or negative. This is likely due to remaining levels of PRX-102 that escaped antibody suppression and were sufficient to break down GL-3. Antibodies found were not anti-glycan nor anti-PEG but mostly directed toward the core of the enzyme. The 20% immunogenicity compares to Fabrazyme and Replagal at 79%[5] and 25%-45%, respectively. Antibodies are frequently cross reactive in patients that use both Fabrazyme and Replagal[6] but do not materially impact the efficacy of the drug.

Data from the interim analysis of the BRIDGE Study was included in the PRX-102 BLA submission to the FDA under the Accelerated Approval pathway. Now that final analysis is available, the data will be used to support a Marketing Authorization Application (MAA) with the EMA. Announced on February 10, 2021, Protalix and Chiesi Global Rare Diseases presented the above key data from the final analysis of BRIDGE at the 17th Annual WORLDSymposium. Dr. Ales Linhart, MD of Charles University presented.

Shareholder Letter

On December 30, 2020, President and CEO of Protalix, Dror Bashan, issued a letter to shareholders. In the letter, he highlighted the progress made with partner Chiesi in submitting the BLA for PRX-102, and the FDA's acceptance and filing of the application under Accelerated Approval and granting of Priority Review designation. Bashan updated investors on the revised Prescription Drug User Fee Act (PDUFA) date to April 27, 2021 and reiterated the potential market for PRX-102 in Fabry and clinical progress, specifically final result reporting from BRIDGE, topline data expected from BRIGHT 1Q:21, and interim results from BALANCE in 1H:21. Finally, he guided toward the 2H:21 commercialization of PRX-102 pending BLA approval.

Bashan acknowledged the expansion of partnerships and collaborations. In July 2020, Protalix entered into a non-binding term sheet with SarcoMed USA Inc., which would support development and commercialization of PRX-110 in pulmonary sarcoidosis and related diseases. An update on this relationship on February 11 executed a non-binding term sheet between the two companies. In March 2020, Protalix announced an agreement with Kirin Holdings Company, Ltd. to conduct feasibility study for production of a novel complex protein using ProCellEx.

The letter summarized the financing achieved during 2020 including a $44 million raise in March through the sale of common stock and warrants in private placement. Other items of note include Protalix' establishment of an at-the-market (ATM) facility through Bank of America Securities that provides the opportunity to raise up to $30 million and the addition of Dr. Yael Hayon to Protalix' senior executive management team as VP Research and Development.

[4] Neutralizing antibodies are distinguished from binding antibodies in that neutralizing antibodies bind to sites (epitopes) directly involved in the activity of the antigen (such as a receptor), interfering with the activity of the antigen, while binding antibodies attach to non-critical portions of the antigen.
[5] Provided in FDA Label for Fabrazyme.
[6] Linthorst, G.E. *et al.* Enzyme therapy for Fabry disease: Neutralizing antibodies toward agalsidase alpha and beta. Kidney International; Volume 66, Issue 4, October 2004, Pages 1589-1595

Summary

Since our recent initiation on Protalix, the company has provided several updates including closing a $40 million raise, partnership with SarcoMed USA, issuance of a 2020 Letter to Shareholders, and announcement of final results from the BRIDGE trial. We also anticipate positive news from the FDA regarding approval of PRX-102. Assuming FDA approval of the candidate by the current target action date in late April, sales of the enzyme should be underway by 2H:20. Below we summarize the key elements of our thesis:

- **PRX-102 on cusp of commercialization**
  - **Target action date: April 27, 2021**
- **Potential for superiority vs market leader Fabrazyme**
  - **Improved efficacy**
  - **Longer duration between infusions**
- **Existing sales and royalty revenues from taliglucerase alfa**
  - **Pfizer, globally**
  - **Fiocruz, Brazil**
- **Maintain regulatory approved plant based expression system**
- **Orphan indication for PRX-102**
- **Partnership with Chiesi for global commercialization of PRX-102 in Fabry Disease**
- **Rights to milestones and royalties**

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PROJECTED FINANCIALS

Protalix Biotherapeutics, Inc. - Income Statement

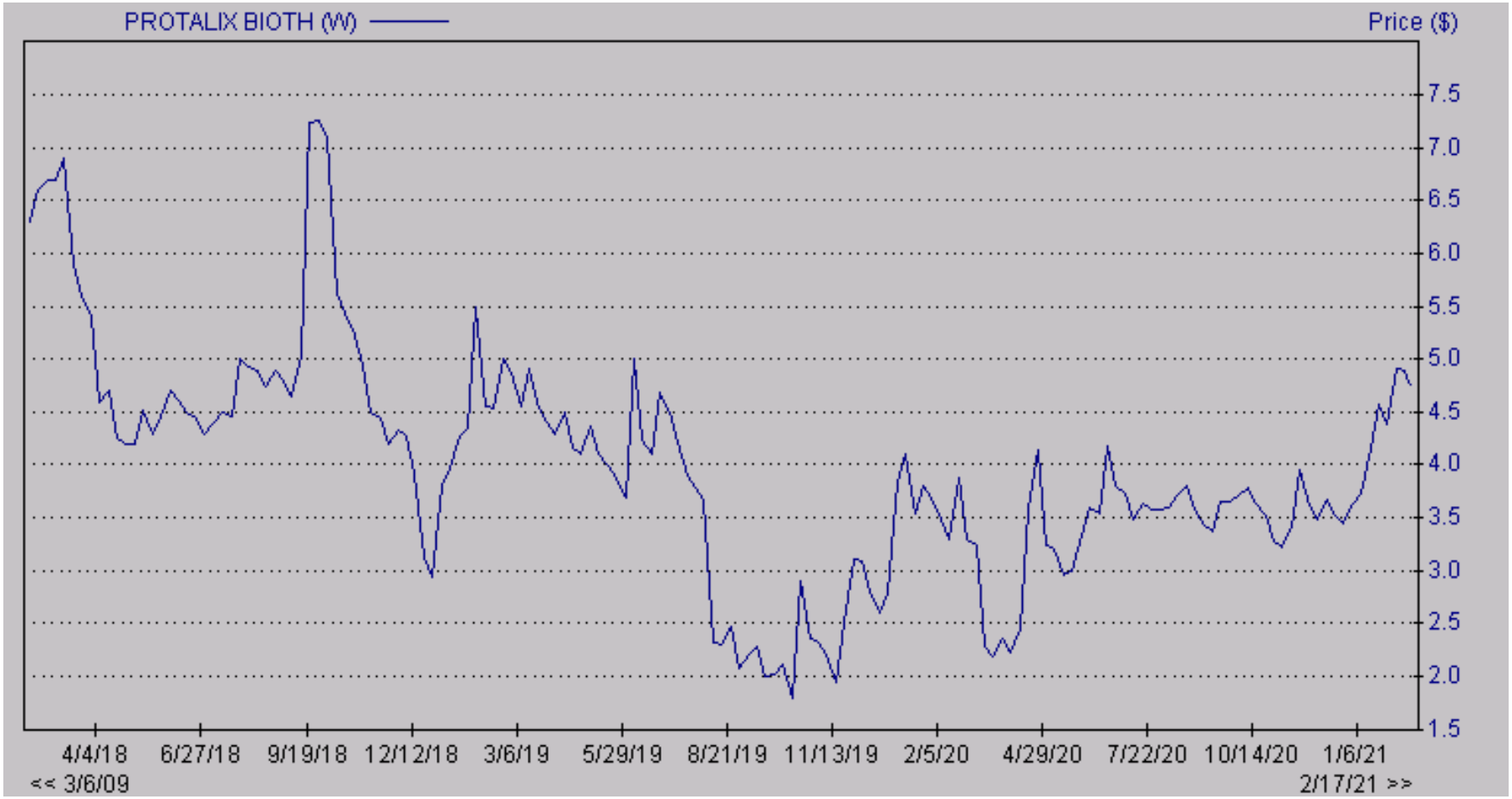
Protalix Biotherapeutics	2019 A	Q1 A	Q2 A	Q3 A	Q4 E	2020 E	2021 E	2022 E
Total Revenues ($US '000)	**$54,693**	**$21,646**	**$10,967**	**$10,790**	**$10,556**	**$53,828**	**$48,939**	**$78,417**
YOY Growth	60%	107%	-10%	-24%	-41%	-2%	-9%	60%
Cost of Revenues	$10,895	$3,426	$1,827	$2,868	$2,919	$11,040	$11,339	$12,638
Product Gross Margin	31.3%	31.9%	49.9%	13.0%	33%	32%		
Research & Development	$44,616	$10,340	$9,186	$7,688	$7,500	$34,714	$19,400	$15,000
Selling, General & Admin	$9,899	$3,187	$2,194	$2,816	$2,560	$10,757	$11,457	$10,510
Income from operations	($10,717)	$4,693	($2,240)	($2,582)	($2,423)	($2,683)	$6,743	$40,269
Operating Margin	-20%	22%	-20%	-24%	-23%	-5%	14%	51%
Financial Expenses	$7,966	$3,229	$1,948	$1,973	$1,950	$9,100	$7,350	$0
Financial Income	($407)	($203)	($38)	($118)	($100)	($459)	($400)	($200)
Pre-Tax Income	($18,276)	$1,667	($4,150)	($4,437)	($4,273)	($11,324)	($207)	$40,469
Net Income	**($18,276)**	**$1,667**	**($4,150)**	**($4,437)**	**($4,273)**	**($11,324)**	**($207)**	**$40,469**
Net Margin	-33%	8%	-38%	-41%	-40%	-21%	0%	52%
Reported EPS	**($1.23)**	**$0.10**	**($0.13)**	**($0.14)**	**($0.13)**	**($0.39)**	**($0.01)**	**$1.06**
Basic Shares Outstanding	14,838	17,381	32,443	32,864	33,300	28,997	34,850	38,200

Source: Company Filing // Zacks Investment Research, Inc. Estimates

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HISTORICAL STOCK PRICE

Protalix Biotherapeutics, Inc. – Share Price Chart



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