Zacks Small-Cap Research

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Protalex, Inc.

(PRTX-OTCQB)

PRTX: We See Big Potential For PRTX-100 In Both RA and ITP…

Current Recommendation	**Buy**
Prior Recommendation	N/A
Date of Last Change	12/1/2014
Current Price (04/24/2015)	$5.50
Target Price	**$10.00**

UPDATE

Having reported the final data from study PRTX-100-104, the company is looking ahead to initiating a Phase 2 study in RA with PRTX-100 in 2015. In addition, in 2015 the company also plans to initiate a clinical trial of PRTX-100 in idiopathic thrombocytopenic purpura (ITP), a rare autoimmune bleeding disorder.

We continue to be optimistic on the future for Protalex with PRTX-100 in both RA and ITP. We believe there are a number of catalysts on the horizon that could send the shares higher in 2015. Our target is $10.

SUMMARY DATA

52-Week High	**$9.00**
52-Week Low	**$4.00**
One-Year Return (%)	**-35.22**
Beta	**2.70**
Average Daily Volume (sh)	**1,668**
Shares Outstanding (mil)	**29**
Market Capitalization ($mil)	**$158**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**14**
Insider Ownership (%)	**81**
Annual Cash Dividend	**N/A**
Dividend Yield (%)	**N/A**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2015 Estimate	**N/A**
P/E using 2016 Estimate	**N/A**

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

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Aug)	Q2 (Nov)	Q3 (Feb)	Q4 (May)	Year (May)
2014	0 A	0 A	0 A	0 A	0 A
2015	0 A	0 A	0 A	0 E	0 E
2016					0 E
2017					50 E

Earnings per Share
(EPS is operating earnings before non-recurring items)

	Q1 (Aug)	Q2 (Nov)	Q3 (Feb)	Q4 (May)	Year (May)
2014	-$0.08 A	-$0.05 A	-$0.18 A	-$0.13 A	-$0.45 A
2015	-$0.15 A	-$0.15 A	-$0.06 A	-$0.11 E	-$0.46 E
2016					-$0.33 E
2017					$0.92 E

Update In RA

In November 2014, Protalex announced data from Cohorts 1 through 5 of the Phase 1b study-104 were presented at a poster session at the American College of Rheumatology (ACR) and the Association for Rheumatology Health Professionals (ARHP) Annual Meeting 2014. Below is our analysis of that presentation:

Brief Background of Study PRTX-100-104

Study-104 was designed to test PRTX-100, a highly purified form of Staphylococcal A (SpA) protein, for the treatment of patients with active rheumatoid arthritis (RA). The primary endpoint was the safety and tolerability of PRTX-100, with secondary objectives examining the effects of the drug on disease activity, assessing the immunogenicity and evaluating the pharmacokinetic (PK) parameters after repeated doses, and determining possible relationships between the immunogenicity of PRTX-100 and safety, PK, and efficacy parameters.

SpA is a 42 kilodalton bacterial membrane protein composed of five nearly identical domains. Each of the domains is capable of disrupting the activity of antibodies and B-cell receptors. SpA is capable of binding the Fc region of human IgG and the Fab framework region of antibodies from the VH3 gene family. This binding produces small complexes of SpA and IgG that are capable of inducing "alternatively activated" or "regulatory" macrophages that have an anti-inflammatory phenotype. Additionally, SpA is capable of interacting with VH3 B-cells and inducing apoptosis.

Previous Phase 1 dose-escalation studies of PRTX-100 have shown it to be safe and well tolerated at doses up to 1.5 µg/kg. Study-104 was designed to test weekly doses of PRTX-100 at 1.5, 3.0, 6.0, and 12.0 µg/kg in Cohorts 1 through 4. A fifth cohort of patients was dosed with weekly doses of either 420 µg PRTX-100 (12 patients), 240 µg PRTX-100 (3 patients), or placebo (5 patients) and then continued with four monthly "maintenance" doses at weeks 8, 12, 16, and 20. For comparison sakes, a 70 kg patient in Cohorts 1 through 4 would have received 105 µg, 210 µg, 420 µg, or 840 µg of PRTX-100 per dose. Protalex had previously presented data on Cohorts 1-4 at EULARs Annual European Congress of Rheumatology in June 2014. The data show that PRTX-100 was safe and well tolerated at the tested doses and that, while the number of patients treated was small, there appeared to be a treatment response.

The data presented for Cohort 5 included pharmacokinetic analysis, evaluation of anti-drug antibodies (ADAs), and disease activity assessed using the American College of Rheumatology (ACR) response. The ACR score is a number indicating to what degree a patient's rheumatoid arthritis has improved based on guidelines set forth by the ACR. The ACR score represents a percentage, with an ACR50 score meaning that a patient's RA has improved by 50%. ACR20 and ACR70 scores are also typically reported in clinical studies of RA treatments.

To qualify for an ACR50 score, a person with RA must have at least 50% fewer tender joints and at least 50% fewer swollen joints at assessment vs. baseline. In addition, the person must show a 50% improvement in at least three of the following five areas: 1) the person's overall assessment of his or her own RA, 2) the physician's global assessment of the person's RA, 3) the person's assessment of his or her own pain, 4) the person's assessment of his or her own physical functioning, and 5) the results of an erythrocyte sedimentation rate or C-reactive protein blood test (both of which test for inflammation).

Pharmacokinetic analysis of Cohort 5 PRTX-100 administration

The following table shows a summary of the pharmacokinetic parameters for PRTX-100 after a 20-minute intravenous infusion of either 240 µg or 420 µg of PRTX-100. Cmax is the maximum serum concentration of PRTX-100 while Tmax is the time, in hours, which it takes to reach the maximum serum concentration. This data is quite comparable to the 3.0 µg/kg and 6.0 µg/kg data seen in Cohort's 1-4. The decrease in Cmax between Days 1 and 22 was also seen in Cohort's 1-4.

Parameters[a]	PRTX-100 dose 240 μg	420 μg
Day 1		
C_{max}, ng/mL	77.3 ± 42.7 (3)	144 ± 44.6 (10)
T_{max}, h	0.38 (3) [0.00–0.58]	0.48 (10) [0.38–1.08]
Day 22		
C_{max}, ng/mL	47.4 ± 37.6 (3)	114 ± 41.2 (8)
T_{max}, h	0.38 (3)	0.38 (8)

Source: Protalex, Inc.

Analysis of anti-drug antibody development

PRTX-100 is a foreign protein, thus it is not surprising that immunization with the compound would lead to the development of ADA's. The following table shows the number of patients in Cohorts 1-5 that were positive for IgG ADA's. Interestingly, even though patients in Cohort 5 received four additional monthly doses of PRTX-100, the rate of ADA formation was very similar when compared to patients in Cohort's 1-4 (64.3% vs. 57.7%).

	Number of patients positive for IgG ADA					
Treatment Dose	PRTX-100 240 μg	PRTX-100 420 μg	PRTX-100 240 μg and 420 μg	PRTX-100 Cohorts 1–4	PRTX-100 All	Placebo All
No. of subjects	3	12	15	31	46	15
Day 22 / 29 [1]	2 / 3 (66.7%)	7 / 8 (87.5%)	9 / 11 (81.8%)	19 / 27 (70.3%)	28 / 38 (73.7%)	0 / 13
Day 57	1 / 2 (50.0%)	5 / 7 (71.4%)	6 / 9 (66.7%)	19 / 28 (67.9%)	25 / 37 (67.6%)	0 / 13
Day 169 [2]	2 / 3 (66.7%)	7 / 11 (63.6%)	9 / 14 (64.3%)	15 / 26 (57.7%)	24 / 40 (60.0%)	0 / 12

Source: Protalex, Inc.

In addition to the development of IgG ADA's, the development of IgE ADA's was also assessed. The development of these antibodies can trigger an allergic response such as anaphylaxis. No patients in Cohort 5 developed detectable IgE ADA's while 5/30 patients in Cohorts 1-4 developed them. However, no patient who tested positive for IgE ADA's ever developed respiratory problems or anaphylaxis, and the five patients who were deemed positive for IgE ADA's had IgE levels just above the lower limit of detection for the assay.

Lastly, the relationship between the development of IgG ADA's and ACR20 response on day 57 and day 169 was examined. There did not appear to be any effect on ACR20 response due to the presence of IgG ADA's, as the following table shows that similar percentages of antibody negative and antibody positive patients experienced ACR20 responses across all cohorts on both days.

	Treatment					
	PRTX-100 Cohorts 1–4 (n=31)		PRTX-100 Cohort 5 (n=15)		PRTX-100 All Cohorts (n=46)	
Summary	Antibody Positive	Antibody Negative	Antibody Positive	Antibody Negative	Antibody Positive	Antibody Negative
ACR20						
Day 57	9 / 18 (50.0%)	4 / 9 (44.4%)	4 / 6 (66.7%)	1 / 2 (50.0%)	13 / 24 (54.2%)	5 / 11 (45.5%)
Day 169	6 / 15 (40.0%)	4 / 11 (36.4%)	3 / 5 (60.0%)	3 / 5 (60.0%)	9 / 20 (45.0%)	7 / 16 (43.8%)

Source: Protalex, Inc.

RA disease activity

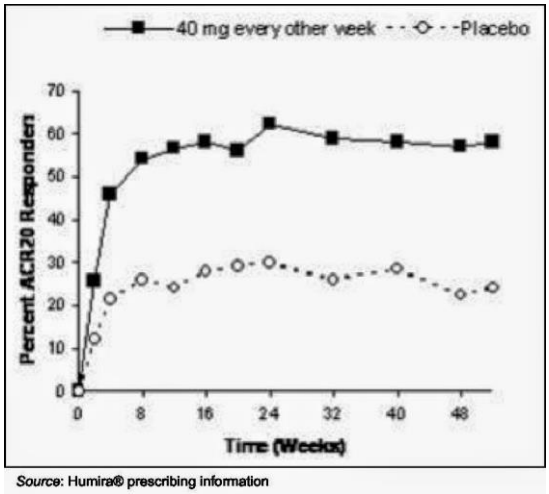
As we mentioned in our initial analysis of the Cohort 1-4 data in June 2014, it is difficult to ascertain any clear signals of efficacy, as the numbers of patients treated was quite low. However, we feel it is still useful to examine the data and compare it to results that are seen with the other biological treatments of RA such as AbbVie's Humira®, Amgen's Enbrel®, and J&J's Remicade® - all blockbuster products with sales in the multi-billions of dollars. We will restrict our analysis to the group of patients from Cohort 5 that were administered 420 µg per dose, as this group comprised most of the patients in Cohort 5 and they appeared to have the most interesting results.

The following table shows the two month ACR20, ACR50, and ACR70 values for Cohort's 1-5 along with the ACR20 data for up to six months.

	Treatment				
	PRTX-100				Placebo
	240 µg	420 µg	Cohorts 1–4 [2]	All	All
No. of subjects [1]	3	9	29	41	15
Day 57 ACR20	2 / 3 (66.7%)	4 / 8 (50.0%)	14 / 28 (50.0%)	20 / 39 (51.3%)	5 / 13 (38.5%)
Day 57 ACR50	0 / 3	1 / 9 (11.1%)	8 / 27 (29.6%)	9 / 39 (23.1%)	2 / 13 (15.4%)
Day 57 ACR70	0 / 3	1 / 9 (11.1%)	3 / 28 (10.7%)	4 / 40 (10.0%)	0 / 12
ACR20					
Day 15	1 / 3 (33.3%)	3 / 8 (37.5%)	6 / 28 (21.4%)	10 / 39 (25.6%)	4 / 13 (30.8%)
Day 29	2 / 3 (66.7%)	4 / 8 (50.0%)	8 / 28 (28.6%)	14 / 39 (35.9%)	4 / 13 (30.8%)
Day 57	2 / 3 (66.7%)	4 / 8 (50.0%)	14 / 28 (50.0%)	20 / 39 (51.3%)	5 / 13 (38.5%)
Day 85	1 / 1 (100%)	5 / 9 (55.6%)	14 / 29 (48.3%)	20 / 39 (51.3%)	4 / 10 (40.0%)
Day 113	2 / 3 (66.7%)	5 / 7 (71.4%)	10 / 25 (40%)	17 / 35 (48.6%)	4 / 11 (36.4%)
Day 169	1 / 2 (50.0%)	5 / 6 (83.3%)	7 / 22 (31.8%)	13 / 30 (43.3%)	5 / 8 (62.5%)

Source: Protalex, Inc.

Approximately 50% of patients from Cohorts 1-5 achieved ACR20 two months after treatment began (Day 57). This is quite comparable to ACR20 response rates seen in patients treated with Humira®, as shown in the following graph.



Source: Humira® prescribing information

In addition to comparing quite favorably to the Humira® ACR20 response rates at two months, the six month ACR20 response rate for Cohort 5 patients dosed with 420 µg PRTX-100 is quite similar to the ACR20 response rates seen with Humira®, Enbrel®, and Remicade®.

ACR20 at 6 months

	Humira®	Enbrel®	Remicade®	Cohort 5 420 µg
No. Patients	207	59	86	6
Dose	40 mg	50 mg	3 mg/kg	0.42 mg
Frequency	Bi-weekly	Weekly	0, 2, 6 wks then bi-monthly	Weekly
Duration	Continuous	Continuous	Continuous	5 weeks + 1x/mo. 4 mo.
ACR20	63%	71%	50%	83%

Sources: Protalex, Inc.; Humira®, Enbrel®, Remicade® prescribing information

There are a couple of points to keep in mind when comparing the data between PRTX-100 and the leading biologic treatments for RA:

1) Study-104 was a very small trial (n=6). This is in comparison to the Phase 3 trials for Humira®, Enbrel®, and Remicade® that contained 207, 59, and 86 patients, respectively. In addition, each of the biologics was tested in at least one other Phase 3 trial that showed very similar results for each of those products.

2) Keeping in mind that it was a very small number of patients, it is still quite encouraging to see such a high ACR20 response rate in the PRTX-100 Cohort 5 group.

3) The amount of drug needed to achieve the ACR20 response rate at six months in the PRTX-100 treated patients is at least two orders of magnitude less than the amount of drug needed for ACR20 responses when treating with Humira®, Enbrel®, or Remicade®.

	Dose	# Doses[a]	Total Amt. Drug
Humira®	40 mg	12	480 mg
Enbrel®	50 mg	24	1200 mg
Remicade®	210 mg[b]	5	1050 mg
PRTX-100[c]	0.42 mg	9	3.8 mg

[a]number of doses in 6 months of treatment
[b]assuming 70 kg patient
[c]includes 4 monthly 'maintenance' doses

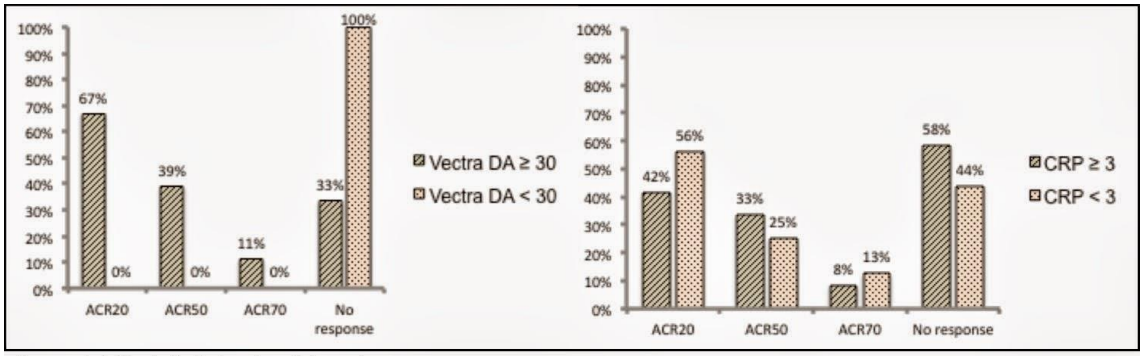
In addition, the cost of goods to produce PRTX-100 is going to be at least 100 times less than for Humira®, Enbrel®, or Remicade®, which means that: A) PRTX-100 could be brought to market in less developed areas of the world where most individuals cannot afford the $30,000 or more per year it costs to be treated with Humira®, Enbrel®, or Remicade® and B) PRTX-100 could be utilized in conjunction with Humira®, Enbrel®, or Remicade® as an inexpensive add-on therapy.

Potential for personalized medicine approach to RA therapy

Lastly, data was presented on a post-hoc analysis of patient samples from Cohorts 1-4 utilizing the Vectra DA score. Vectra DA is a quantitative laboratory test that is validated to assess RA disease activity and was developed by Crescendo Bioscience, which was acquired by Myriad Genetics (MYGN) in February 2014. The test uses the concentration of 12 biomarkers in the blood and a proprietary algorithm to derive a score from 0-100. These 12 biomarkers were found to have the best ability to evaluate RA disease activity in multiple studies of over 1,100 patients. The Vectra DA score classifies RA into low (1-29), intermediate (30-44), or high (45-100) disease activity.

Protalex performed post-hoc analysis of data from Cohorts 1-4 to show that by grouping patients according to Vectra DA score they could improve trial efficacy outcomes. The Vectra DA score was determined using a blood specimen collected when the patients first entered the trial. Specifically, the data showed that three patients entered the trial with low Vectra DA scores (12, 19, 21; all three patients had DAS28-CRP scores > 5) and that none of these three patients responded to treatment with PRTX-100. In contrast, 66.7% of patients with Vectra DA scores > 30 (intermediate or high disease activity) had at least an ACR20 response, as shown in the following graph.

Grouping patients by c-reactive protein (CRP) value did not result in the same outcome.



Source: David Bautz, Zacks Investment Research

While this data does look rather encouraging, the fact remains that the Vectra DA test was only able to remove three patients from Cohorts 1-4 who did not have a score ≥ 30. In addition, this was a post-hoc analysis that may be identifying a pattern that only exists in this cohort of patients and may not be replicated in a larger clinical trial. That being said, if this trend holds up in a larger, prospective analysis we can foresee the Vectra DA test being utilized as a screening tool to predict whether or not a patient is likely to respond to treatment with PRTX-100. There is currently no personalized approach to RA treatment; in essence a patient is started on one treatment and if they do not respond they are transitioned onto another treatment option until their disease is under control. We can envision how having a validated test that could predict who is most likely to benefit from PRTX-100 treatment moving it to front-line status. This would be all the more likely if future clinical trials continue to show PRTX-100 to be safe, well tolerated, and efficacious, particularly when compared to Humira®, Enbrel®, or Remicade®.

Awaiting next steps in RA

In April 2015, Protalex announced final cohort analysis from the Phase 1b trial. The final analysis confirmed the previously reported safety and tolerability of the drug. The analysis also suggests that weight-based dosing and monthly maintenance doses are an important aspect of the protocol and should be considered for future trials with PRTX-100. With respect to the relationship between certain biomarkers and response to PRTX-100, management is now going back and re-examining the data from the South African -103 study. In addition to working with outside consultants, the company is also speak to various “Big Pharma” companies in order to obtain feedback on the design of the Phase 2 trial such that the results will be of interest to potential partners at pharmaceutical companies.

Management expects to complete this analysis and then determine the next steps for PRTX-100 in RA sometime this summer. We feel like PRTX-100 is not far enough along in clinical development for a large pharmaceutical company to want to enter into a partnership yet, thus Protalex wants to be sure that whatever data is generated in the Phase 2 trial will be sufficient for a large pharmaceutical company to decide whether or not PRTX-100 is worth pursuing further. We also believe the more data management has with respect to the biomarker activity of the drug, the more likely a big pharma partner will be interested in moving the drug forward because the probability of success goes up as the target population becomes more defined.

Update In ITP

On March 31, 2015, Protalex, Inc. (PRTX) announced that the U.S. Food and Drug Administration (FDA) has cleared the initiation of a Phase 1/2 study with PRTX-100, the company's formulation of a proprietary, highly purified form of Staphylococcal Protein A (SpA), in patients with Immune Thrombocytopenia (ITP). The company filed an Investigational New Drug (IND) application for the start of this trial earlier in the year. We expect that the trial will begin in the second quarter 2015.

Background on ITP

ITP is a bleeding disorder characterized by bruising and increased bleeding as a result of immune-mediated accelerated destruction of platelets and impaired production of platelets. ITP is an autoimmune-mediated condition in which the body's own immune system attacks and destroys platelets. The disease can be brought on by bacterial or viral infections. The condition can be acute (short-term) or chronic (long-lasting) in nature, with women being two to three times as likely to develop chronic ITP as men. The bleeding can be found inside the body (internal bleeding), and underneath or from the skin (external bleeding). Signs of bleeding may include:

→ Bruising or purplish areas on the skin or mucous membranes (such as in the mouth). These bruises are called purpura. Purpura are caused by bleeding under the skin, and they may occur for no known reason.
→ Pinpoint red spots on the skin called petechiae. These spots often are found in groups and may look like a rash. Bleeding under the skin causes petechiae.
→ A collection of clotted or partially clotted blood under the skin that looks or feels like a lump. This is called a hematoma.
→ Nosebleeds or bleeding from the gums (for example, during dental work).
→ Blood in the urine or stool (bowel movement).



The diagnosis of ITP is based upon a low platelet count, usually less than 100,000 per microliter of blood, in the absence of other possible causes of reduced platelet numbers such as an underlying illness or medication. A normal platelet count is considered to be between 150,000 and 450,000 per microliter. ITP is recognized by the FDA as an orphan disease, which is defined as a condition that affects fewer than 200,000 people nationwide. The incidence for ITP is approximately 9.5 per 100,000 people in the U.S., representing approximately 30,000 cases.

Current treatment options for ITP

There are a number of treatment options available for ITP patients depending upon the severity of symptoms and whether the patient is newly diagnosed or has a chronic condition. Treatment is typically recommended for adult patients who have significant bleeding and is not necessarily tied to an absolute platelet counts threshold, although bleeding accompanied with a platelet count < 50,000 per microliter warrants treatment.

✓ **Glucocorticoids**: These agents work by suppressing the immune system. In urgent situations, infusions of dexamethasone or methylprednisolone may be used, while less severe cases can typically be treated with oral prednisone or prednisolone. As a patients platelet count increases the glucocorticoids are gradually tapered back to limit side effects of long-term glucocorticoid use, which include osteoporosis, cataracts, and diabetes. Relapse rates are high with glucocorticoid treatment, as only 20-40% of patients will have a durable remission (Stevens *et al*., 2006).

- ✓ **Intravenous Immunoglobulin**: Another treatment option for urgent situations is the use of intravenous immunoglobulin (IVIg), which contains the pooled, polyvalent IgG antibodies extracted from over a thousand healthy donors. The mechanism of action for IVIg in autoimmune diseases is currently unknown, but the treatment is considered relatively safe although serious side effects have been reported, including anaphylaxis and venous thrombosis.

- ✓ **Thrombopoietic agents**: These medications work to directly stimulate production of platelets; however, unlike other treatment options they do not appear to have an effect on platelet destruction. Two of these agents are currently available:

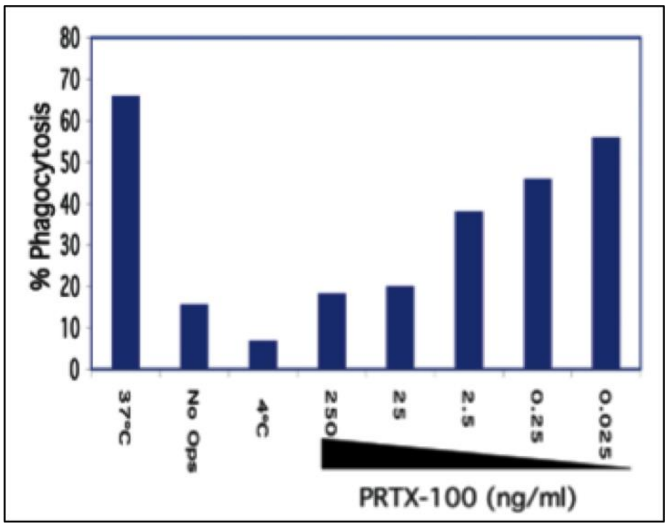
  - → Romiplostim (Nplate®): This is an Fc-peptide fusion protein that increases platelet production by binding to and activating the thrombopoietin (TPO) receptor. Clinical trials showed romiplostim to be effective in chronic ITP patients, particularly in those with relapsed disease who had previously had a splenectomy (Kuter *et al*., 2010). The FDA approved the compound in 2008. Amgen reported revenues of $469 million for Nplate® in 2014.

  - → Eltrombopag (Promacta®): This is an oral TPO receptor agonist that induces megakaryocyte proliferation and differentiation from bone marrow progenitor cells. Clinical trials showed eltrombopag decreased bleeding episodes and increased platelet count in a dose dependent manner (Bussel *et al*., 2007). The FDA approved the compound in 2008. GlaxoSmithKline reported revenues of approximately $340 million for Promacta® in 2014.

PRTX-100 for the treatment of ITP

Given the high relapse rate associated with current ITP medications, there exists a significant unmet medical need for additional and effective ITP treatments. While successful in treating ITP patients, neither of the thrombopoietic drugs impacts the principal pathological mechanism of ITP, namely the destruction of platelets.

Protalex believes that PRTX-100 may have a more direct impact on ITP by limiting the destruction of platelets, thus complementing or perhaps even reducing the use of thrombopoietic agents. Research presented at the 2006 Annual meeting of the American Society of Hematology showed that PRTX-100 inhibited the phagaocytosis of platelets in an *in vitro* assay in a dose dependent manner, as shown in the following chart.



Source: Protalex, Inc.

The assay consisted of labeling platelets with an antibody, thus signaling for the platelets to be destroyed through phagocytosis. This is similar to what occurs in a patient with ITP. Interestingly, when monocytes were treated with either 25 or 250 ng/mL PTRX-100 prior to exposure to antibody-bound platelets, the level of platelet phagocytosis was similar to that seen when platelets were not labeled with antibody ("No Ops" group), indicating that PRTX-100 eliminated most antibody-mediated phagocytosis.

Additional support for the use of PRTX-100 in ITP comes from previous studies showing the effectiveness of the Prosorba® column in treating ITP patients (Snyder *et al*., 1992). The Prosorba column is a medical device containing highly purified SpA covalently bound to a silica matrix. The device is used in conjunction with a plasmapheresis machine. In this *ex vivo* treatment, blood is withdrawn from the patient, cells are separated from plasma in the machine, and the plasma is passed through the Prosorba column. The plasma is then recombined with the cells and returned to the patient.

In the study by Snyder *et al*., a total of 72 ITP patients with platelet counts < 50,000 per microliter and who had failed at least two prior therapies were treated with an average of six Prosorba treatments of 0.25 to 2.0 L of plasma per procedure over a span of two to three weeks. The treatments caused an acute increase in the platelet count to greater than 100,000 per microliter in 18 patients and to 50,000 to 100,000 per microliter in 15 patients. The response was transient in seven of those patients but no additional relapses were reported over a follow up period of up to 26 months. Clinical responses were associated with significant decreases in specific serum platelet auto-antibodies, platelet-associated immunoglobulin, and circulating immune complexes.

The mechanism of action for why the Prosoba® column is effective as an ITP treatment probably has little to do with the binding capabilities of SpA. SpA selectively binds to antibodies that contain the V_H3 antibody heavy chain, which represents most if not all auto-antibodies, including those involved in ITP. However, the IgG antibody content of the human body is about 50 grams total, with 50% turnover every 3 weeks. The FDA approval summary for the Prosorba column states that the antibody absorption capacity is approximately 0.56 g, suggesting that it would be impossible to have a major impact on total IgG load via absorption treatment.

Instead, the efficacy of the Prosorba® column in treating ITP is most likely predicated on the fact that up to 200 µg of SpA can leach from the column during immunoabsorption procedures (Roark *et al*., 2002). The SpA then likely binds to and deletes V_H3 antibodies, including those that are targeting platelets (Silverman *et al*., 2000). It is for this reason what we believe PRTX-100, a highly purified form of SpA, has significant potential in ITP.

Next steps in ITP

Protalex will be testing the efficacy of PRTX-100 in ITP patients in a Phase 1/2 open-label, dose-escalation study that will commence in the second quarter of 2015 (NCT02401061). Previously, Protalex had tested PRTX-100 in a small clinical study in ITP patients in 2008 (PRTX-100b-103 Study) that was never completed due to a difficulty in enrolling patients. The study enrolled nine patients and no side effects or toxicities were noted with repeated weekly doses of PRTX-100 of 0.075 and 0.15 µg/kg before further recruitment of patients was suspended. It is clear that more is known today about PRTX-100 than in 2008; thus, we believe investigator interest in the drug is now high enough that enrollment in the planned 36 patient Phase 1/2 study can be achieved.

The proposed Phase 1/2 study will include patients with chronic ITP who have platelet counts of less than 30,000 per microliter and have failed at least one prior therapy. Concomitant use of corticosteroids or immune suppressive agents will be allowed. The doses being tested will range from 1.0 to 24.0 µg/kg and will be administered as single weekly doses over a four-week period. Approximately three to six patients will be enrolled per dosing cohort. The primary endpoint for the study is platelet response, which is defined as platelet count >30,000 per microliter and at least a doubling of baseline platelet count. We anticipate top-line data from the trial to be reported in mid-2016.

Upon successful completion of the Phase 1/2 study we anticipate the company being able to begin a Phase 3 trial at the end of 2016 or early 2017. Given that ITP is an orphan indication, it is likely that the Phase 3 trial will only need to enroll a few hundred patients. Nplate® was approved based on the results of two clinical trials, one with patients who had not undergone a splenectomy and one with patients who had. However, each trial only enrolled 62 and 63 patients randomized 2:1 to receive either Nplate® or placebo, thus indicating that a very large trial will likely not be necessary for PRTX-100 to gain approval.

Conclusion

We continue to recommend Protalex as we believe the potential for PRTX-100 is quite large, with sales in excess of $1 billion alone for RA in the U.S. The potential in ITP, which we peg to be around $400 million in peak sales, although significantly smaller than what we believe the drug can do in RA, is quite intriguing because ITP is an orphan indication. The company recently filed the Orphan Drug designation application to the U.S. FDA for PRTX-100 in ITP. ODD not only confers rock-solid market exclusivity for Protalex, it also attracts potential pharma partners thanks to strong pricing and accelerated pathways to approval. We expect a response in July 2015.

Protalex is still flying relatively under-the-radar for most biotech investors. Management and insiders own over 80% of the company, and recently made available another $5.0 million in November 2014. We believe that having two clinical programs underway in 2015, one in RA and one in ITP, should help draw investor attention to the name. We see summer 2015 as a "coming out party" for the name, with two significant catalysts: 1) FDA response on the Orphan Drug application in ITP, and 2) advancement into Phase 2 for RA. Also, with a market capitalization of $160 million and a $5.50 stock price, we believe an uplisting to NASDAQ is on the near-term horizon. As more investors become more familiar with the Protalex story, the stock price is likely to reflect the potential we see for PRTX-100. Our financial modeling pegs the valuation around $10 per share.

Protalex, Inc.
Income Statement

Protalex, Inc.	FY 2014 A	Aug-14 A	Nov-14 A	Feb-15 A	May-15 E	FY 2015 E	FY 2016 E	FY 2017 E
PRTX-100 Sales / Royalties	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Licensing / Collaborative	$0	$0	$0	$0	$0	$0	$0	$50.0
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$50.0**
YOY Growth	-	-	-	-	-	-	-	-
CoGS	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
R&D	$3.2	$0.6	$0.9	$0.7	$1.5	$3.8	$5.0	$5.0
SG&A	$8.3	$3.5	$3.2	$0.8	$1.6	$9.1	$7.5	$7.5
Depreciation & Amortization	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	**($11.6)**	**($4.1)**	**($4.1)**	**($1.6)**	**($3.1)**	**($12.9)**	**($12.5)**	**$37.5**
Operating Margin	-	-	-	-	-	-	-	-
Interest & Other Income	($0.3)	($0.1)	($0.1)	($0.1)	($0.1)	($0.3)	($0.5)	($0.5)
Pre-Tax Income	($11.9)	($4.2)	($4.2)	($1.7)	($3.2)	($13.2)	($13.0)	$37.0
Taxes & Other	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($11.9)	($4.2)	($4.2)	($1.7)	($3.2)	($13.2)	($13.0)	$37.0
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.45)**	**($0.15)**	**($0.15)**	**($0.06)**	**($0.11)**	**($0.46)**	**($0.33)**	**$0.92**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	26.2	28.8	28.8	28.8	30.0	29.1	40.0	40.0

Source: Zacks Investment Research, Inc. *Jason Napodano, CFA*

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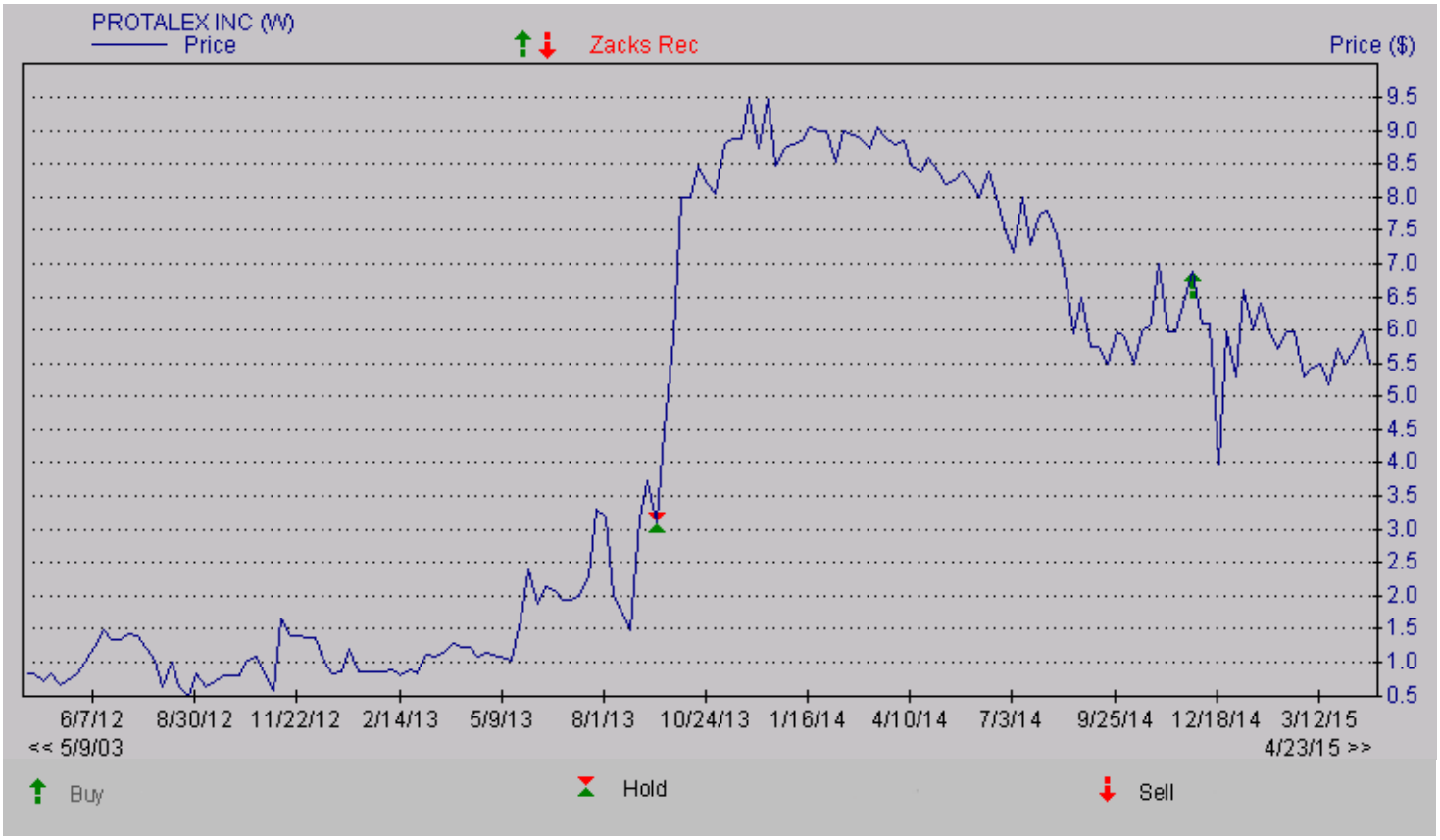

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