A Biotech Superstar Taking off on FDA Approval

Biotech Gems
Progenics: A Great Risk/Reward Play

In this report we’re reviewing a promising small cap biotech/biopharma company called Progenics Pharmaceuticals, Inc. (Nasdaq: PGNX). The stock currently sells for around $6 a share with a market capitalization of $429 million. Based on the potential of its key product, developing pipeline, increasing cash flow, upcoming catalysts as well as the company’s attractiveness as a buyout target PGNX’s shares are easily worth twice the current price of the stock over the next 12-18 months.

Most importantly it just had PDUFA date with the FDA on July 19th where the oral version of its key product was approved. This should exponentially boosting sales and the company’s prospects. More on page 4.

Company Overview:

Progenics Pharmaceuticals, Inc. is developing a number of oncolgical therapeutics and diagnostics in the United States and internationally. Progenics leverages expertise in radiopharmaceutical therapeutics, diagnostic imaging agents, and Prostate Specific Membrane Antigen (PSMA) to pursue a unique, multi-faceted approach to targeting, tracking and treating cancer.

![Stock Chart]

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PGNX Progenics Pharmaceuticals, Inc. Nasdaq: PGNX

Open 6.21 High 6.51 Low 5.83 Close 6.14 Volume 15.8M Chg +1.20 (+24.29%)
Pipeline:

Progenics has a pipeline of 11 products ranging from pre-clinical through late-stage development stages, and with several more products poised to generate revenue relatively soon. Six of the 11 products are focused on critical unmet diagnostic imaging and therapeutic needs of prostate cancer patients, one targets rare neuroendocrine cell tumors, two treat Opioid Induced Constipation, and two are HIV treatments.

Below is a quick rundown of the product and pipeline portfolio. Keep in mind that Relistor is the key product to the company’s near and medium term future and the rest of the pipeline represents multiple “shots on goal” and is “gravy” at Progenics’ current stock price.
**RELISTOR SC (Subcutaneous Injection)**

**What it Does:** Progenic’s first commercial product Relistor SC treats Opioid Induced Constipation (OIC) in patients with advanced illness or chronic pain.

**Key Differentiator(s):** Relistor reverses some of the side effects of opioid drugs such as constipation without affecting pain relief or triggering withdrawals. This medicine is used when laxatives have not worked well. Relistor competes with AstraZeneca’s (NYSE: AZN) product Movantik (which was first to market and is administered orally).

**Phase / Status / Expected Launch:** Relistor SC is Progenics’ most advanced product, approved and being marketed by Valeant Pharmaceuticals International, Inc. (NYSE: VRX) in the United States. Valeant is licensed to market the product worldwide.

**Expected Market:** 3% of U.S. adults are receiving long term opioid therapy and 41% of those (3.7M) develop OIC. Royalties to Progenics for this product have increased nearly 15 fold (to $2.2M from $147k in the prior quarter) and are expected to continue increasing based on the sales compensation structure at Valeant. Additionally, there is more growth potential to market Relistor worldwide.

**Other Considerations:** The injection format is inconvenient and uncomfortable. Financial instability and negative opinions for distribution partner Valeant are likely to temporarily impact product growth and revenue. It is also worth considering that effective marketing options are tricky for a product related to constipation and long term opioid use.

**RELISTOR - Oral**

**What it Does:** This version of Relistor also treats OIC but is administered orally instead of by injection.

**Key Differentiator(s):** Phase II results showed a significantly increased percentage of patients with a natural bowel movement within 4 hours (over existing standards of care). The Oral option will be more convenient and will eliminate a key differentiation point for competitor Movantik. Relistor is currently the only drug approved for OIC under both palliative care and non-cancer pain.

**Phase / Status / Expected Launch:** The NDA was submitted in June 2015. The FDA recently extended the PDUFA review date of the oral Relistor NDA, by three months to July 19, 2016 in order to review additional data related to Progenic’s distribution partner Valeant. The drug was approved on the 19th.

**Expected Market:** The oral therapy targets the same patients as the existing Relistor therapy. Revenues are expected to grow exponentially faster once the oral version of the medication is available. In its last completed quarter, injectable Relistor did over $15 million total sales. Additionally, FDA approval of Relistor oral triggered a $50 million milestone payment from Valeant with opportunities to generate as much as $200 million more in commercialization milestones including $10 million on the first $100 million of calendar year net sales from the Relistor franchise. Progenics also gets 15% to 19% of overall sales of both versions of Relistor as a royalty stream.
**Azedra**

**What it Does:** Azedra is a radiotherapeutic product candidate for the treatment of pheochromocytoma and paraganglioma, very rare tumors that form from neuroendocrine cells. Neuroendocrine cells are primarily in the adrenal glands but are found throughout the body. These cells release hormones into the blood which control heart rate, metabolism, and blood pressure.

**Key Differentiator(s):** There are currently no approved therapies in the U.S. for these very rare diseases. Existing treatments include adrenergic blockade, surgery, chemotherapy, and radiation which generally fail to produce a cure or significant remissions. A product chemically similar to Azedra® with a much lower specific activity and less desirable side effect profile has been used with some success; however, it is not approved by the FDA for the treatment of pheochromocytoma and paraganglioma. Effective alternative therapies are needed, especially in patients who have relapsed. The most recent study saw a more than 50% reduction in anti-hypertensive medications.

**Phase / Status / Expected Launch:** Azedra is currently in Phase IIb clinical trial under special protocol assessment (enrollment is completed). Top Line Data is expected in late 2016 or early 2017 and NDA submission to the FDA is anticipated in the first half of 2017. The FDA granted Breakthrough Therapy designation, Ultra-Orphan Designation (given the rarity of the cancers), and Fast Track Status and has indicated it would grant a full approval instead of conditional approval based on the positive outcome from the phase 2b trial (i.e. no need for confirmatory phase 3 trial). This product has a good chance to hit the market in 2018.

**Expected Market:** Pheochromocytoma and paraganglioma’s prevalence in the U.S. is 3,000-6,000 patients annual (< 1,000 new cases diagnosed annually). Annual sales can be projected in the $225 million range assuming a cost of $200,000 annually per patient for 25% of the eligible patients. As the diseases are very rare and the target market is small, patients will expect to pay more for the therapy. Azedra is the next significant commercial opportunity for Progenics and the company intends to retain the rights and commercialize the drug independently in the U.S.

**Other Considerations:** The U.S. market is reachable with a small specialty sales force targeting major centers where these rare tumors are treated. Commercialization of Azedra should not be a major burden and Progenics plans to hire a small commercial team.

**EXINI Bone BSI**

**What it Does:** Analytical software that assists physicians and patients with analysis of bone scan index from bone scintigraphy images, expected to assist with Prostate Cancer quantification and tracking.

**Key Differentiator(s):** Removes observer variability and reduces the time to quantify the tumor burden of the skeleton. Over time, this product is expected to enhance the other prostate cancer imaging programs in the pipeline (1404 and PyL).

**Phase / Status / Expected Launch:** Approved for use in the EU, Japan and the U.S. Progenics’ goal is to commercialize this product in the U.S. in 2016.
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**Expected Market:** There are approximately 1,100 hospitals in the U.S. and approximately 7,000 in the EU (not counting other types of medical facilities). Prostate cancer is the second most common form of cancer affecting men in the United States: an estimated one in seven men will be diagnosed with prostate cancer in his lifetime. The *American Cancer Society* estimates that each year approximately 220,800 new cases of prostate cancer will be diagnosed and about 27,540 men will die of the disease. Approximately 2.9 million men in the U.S. currently count themselves among prostate cancer survivors.

**Other Considerations:** Acquisition of this product brought with it existing relationships with key European partners, clinicians, and researchers to support late-stage pipeline.

**1404**

**What it Does:** 1404 is a TC (technetium) 99m labeled small molecule diagnostic imaging agent to diagnose and detect prostate cancer.

**Key Differentiator(s):** 1404 targets a specific antigen on the surface of >95% of prostate cancer cells and is more sensitive in detecting cancer Versus an MRI in the Phase II tests. Per patient, there are multiple opportunities to use this imaging agent (i.e. during diagnoses, surveillance, staging, planning/monitoring...) According to a recent study, 40 to 50% of men are choosing active surveillance over treatment and this agent will better support that choice.

**Phase / Status / Expected Launch:** Phase II testing has been completed detecting cancer in the Prostate gland with 94% sensitivity (versus 86% for an MRI). The Company’s goal for this product is to release interim analysis for the pivotal Phase III trial in 2016.

**Expected Market:** Refer to the prostate cancer statistics above.

**Other Considerations:** This product will be enhanced by EXINI BSI in the future.

**PSMA Antibody Radiolabeled With Alpha Emitter**

**What it Does:** This product candidate is a prostate specific membrane antigen (PSMA)-targeted Iodine-131 labeled small radiopharmaceutical molecule which treats metastatic castration resistant prostate cancer.

**Key Differentiator(s):** The company maintains that it has a leadership position in PSMA targeted therapeutics which have the potential to transform clinical practice with improved detection and monitoring of prostate cancer. On May 2nd, the Company announced it had granted Bayer exclusive worldwide rights to develop and commercialize products using Progenics’ PSMA Antibody Technology in combination with Bayer’s Alpha-Emitting Radionuclides.

**Phase / Status / Expected Launch:** In Phase III testing with interim results expected soon in the second half of 2016.

**Expected Market:** Refer to the prostate cancer statistics above. The recent Progenics/Bayer agreement included an upfront payment of $4M, up to additional $49M in potential clinical and...
regulatory development milestones, potential net sales milestone payments up to $230M, and single digit royalties on net sales.

**Other Considerations:** Licensed to buyer.

**PSMA ADC**

**What it Does:** PSMA ADC is an antibody-drug conjugate therapeutic for the treatment of prostate cancer. It binds to a known cancer marker known as prostate specific membrane antigen (PSMA) along with a potent toxin.

**Key Differentiator(s):** According to Progenics, this therapeutic has the potential to transform clinical practice in prostate cancer by selectively attacking tumor cells while sparing healthy tissues. Progenics boasts a leadership position in PSMA targeted therapeutics.

**Phase / Status / Expected Launch:** PSMA ADC has completed Phase II testing in chemotherapy-experienced patients (demonstrating activity and tolerability) and there is an ongoing second PII test in chemotherapy-naive patients.

**Expected Market:** Refer to the prostate cancer statistics above.

**PYL**

**What it Does:** PYL is a PET Radiopharmaceutical imaging agent product candidate targeting a known prostate cancer antigen (PSMA).

**Key Differentiator(s):** The completed pilot study data indicates high uptake even in small lesions, identification of more lesions than the current standard of care, detection of lesions as small as 3mm, tolerance with no serious adverse effects to date, and a few mild adverse effects. This agent has the potential to detect minimal levels of cancer (including some undetectable today such as during early stages) and sites of relapse non-invasively. It finds prostate cancer cells, and is not confounded by degenerative or inflammatory conditions (including recent surgery). Per patient, there are multiple opportunities to use the agent (i.e. during diagnoses, surveillance, staging, planning/monitoring).

**Phase / Status / Expected Launch:** after positive results from the initial study, the next steps are several clinical trials including 2 phase II studies. The company aims to initiate the trials in 2016.

**Expected Market:** Refer to the prostate cancer statistics above.

**Other Considerations:** In-licensed from Johns Hopkins University. This agent will likely also be enhanced by EXINI BSI over time. Over the course of this year, the company plans to further explore how to leverage PyL to support further development of promising therapies in prostate cancer.

**1095**

**What it Does:** 1095 is a targeted small molecule radiotherapeutic which (treats metastatic castration resistant prostate cancer), and selectively binds to PSMA.
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**Key Differentiator(s):** This product candidate delivers a lethal dose of radiation direction to prostate cancer cells with minimal impact on healthy tissue.

**Phase / Status / Expected Launch:** This product is in the clinical stage, early results of the best 25 show reduced PSA levels and bone pain, with potent activity in advanced cancer. The company’s goal is to initiate a Phase I trial in 2016.

Additionally, the company is developing PRO 140, an HIV treatment viral entry inhibitor currently in Phase II testing, and PRO 391, antibodies targeting C. Diff Toxins currently in the pre-clinical stage. These are not expected to impact market valuation of Progenics any time soon.

**Upcoming Catalysts & Balance Sheet:**

The company ended 2015 with just under $75 million in net cash on the balance sheet. Combined with royalties from Relistor and milestone payouts in 2016 especially the expected $50 million payout when the oral version of Relistor is approved as expected in July, the company is in an excellent position to fund development of its pipeline.

The rights to Relistor were owned by **Salix Pharmaceuticals** before it was bought out by Valeant in the first half of 2015. At that time, Salix believed that the peak sales for the injectable and oral versions of Relistor were approximately $1.3 billion annually. If that projection turns out to be wrong by half, the company is severely undervalued on the value of Relistor alone.

Although the distribution rights being owned by Valeant which is currently a pariah in the market complicates a buyout scenario, it does not preclude it. Valeant will need to sell off assets to pay down its debt and its ownership of the Relistor rights is a valuable asset to sell. After the oral version of Relistor being approved I could easily see the likes of **Allergan (NYSE: AGN)** being a bidder for Relistor which could also put Progenics in play as a buyout candidate given their pipeline and the amount of milestone payouts and royalties it will earn over time from Relistor. Even at twice the current price, a purchase should be accretive given Allergan’s or another bigger industry player larger and well established sales forces.

**Analyst Commentary:**

All three analysts who offered recommendations on the company in the past three months issued Buy recommendations with an average price target of $11.33 a share.

On May 6th, Brean Capital reiterated a Buy rating on Progenics with a price target of $14 indicating “We expect a material uptick in royalties upon launch of oral Relistor in 2H16 (July 19 PDUFA), given that Valeant’s 50 rep pain salesforce is compensated on Relistor but not all or most other drugs it sells, in addition to the $50M US approval milestone”.

On April 4th, Needham & Company reiterated a Buy rating and price target of $11.00 despite financial risks associated with Valeant. “A hobbled Valeant may not be the ideal marketing partner, but, in our view, PGNX shares already reflect this.”
According to BTIG analysis, "Progenics...has the potential for a significant rerating in the next 12-18 months."

Outlook:

Progenic’s stock price has been dragged down by ongoing bad news related to its Relistor distribution partner Valeant Pharmaceuticals International, Inc. However, if the company receives the widely expected FDA approval of RELISTOR ORAL by July 19th 2016 and earns the milestone payment from Valeant that will continue to fuel its pipeline growth (or forges a new similar distribution partnership arrangement should Valeant default) the risk that is currently built into its price is likely to evaporate quickly. Analyst consensus is that the stock is slightly undervalued based on a solid cash position and the promise of Relistor and Azedra in the near term.

Recommendation:

**Buy PGNX** with a price target range over next 12-18 months $10 to $12 a share for a 60% to 100% gain.

Editor Position: Long PGNX