

Post-Election Rally Brings Optimism

Thanksgiving came a few weeks early for biotech investors in 2016. The unexpected “clean sweep” by Republicans ignited a huge rally in this beaten down sector of the market. Both the pharma and biotech industries, as well as their shareholders, had been quite fearful of significant new harmful legislation and regulation if the Senate, and to a lesser extent the House of Representatives, had turned over. Bad actors in the industry like **Valeant Pharmaceuticals (NYSE: VRX)** should continue to come under scrutiny, but stringent new rules that could stifle innovation and hinder business models in the industry seem off the table for now. This is something the sector celebrated with great glee.

The week after the election, the biotech sector had its best weekly performance in more than 15 years. We did give back a tiny bit of that large rally this week as the sector consolidated somewhat and some profit taking occurred, which was more than understandable. Interestingly, small caps continue to outpace their larger brethren by a significant margin in regards to performance.

Part of this is thanks to small caps across the market being strong performers ever since Donald Trump’s surprising election and the correlated rise in the dollar which will squeeze the profits of large multi-nationals further. The Russell 2000 is up nearly 14% over the past two weeks or so, an impressive performance to say the least.

Small and mid-cap biotech and biopharma concerns are also rising on renewed hopes of increased M&A activity across the industry now that the election has resulted in political certainty. In addition, financing rates remain low and drug and biotech giants still need to replenish their pipelines which provides a nice backdrop for increased purchase activity. Any sort of “tax holiday” that allows larger firms to bring home some of the over \$2 trillion squired away overseas at a reduced tax rate could throw another log on that fire as well. Biotech and pharma concerns in general are very cash rich and have substantial funds located outside the country in their foreign operations.

After the significant post-election rally, we are now back up near the top end of a trading range for the sector, which had been in place since the market bottomed in February. Given that third quarter earnings season is pretty much over, I think we need to see increased acquisition activity to move substantially higher. This is something that we will be watching closely with Biotech Gems through yearend. If much rumored mid-caps like **Biomarin Pharmaceuticals (NASDAQ: BMRN)**, **Incyte (NASDAQ: INCY)** or **Ionis Pharmaceuticals (NASDAQ: IONS)** get bought out at significant premiums, I think the sector could easily have a substantial rally from current levels.

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We have several names within the small and mid-cap part of the Biotech Gems portfolio that would make logical acquisition candidates should the “animal spirits” start to flow again in the M&A space. **Synergy Pharmaceuticals (NASDAQ: SGYP)** and **Acadia Pharmaceuticals (NASDAQ: ACAD)** are probably the two most mentioned right now in regards to buyout rumors.

One thing is for sure, whether there is pickup in M&A deals or not, the outlook for the biotech sector does seem much brighter than it did just a month ago.

Thank You and Happy Hunting



Bret Jensen
Editor
Biotech Gems

Trevena Inc. (NASDAQ:TRVN)

Our next Biotech Gems recommendation is a name I am familiar with and made a quick 100% profit on in a speculative trade more than a few years ago. Since then, the company has made significant progress developing its pipeline. The name has seen some insider buying in its shares recently, which is always a nice vote of confidence.

Ironically, the stock is back down near the levels I originally purchased it at for a "quick trade", and is looking more like a longer-term investment now with a favorable and attractive risk to reward profile worthy of inclusion into the Biotech Gems portfolio. It will be replacing **Synthetic Biologics (NYSE: SYN)**, whose pipeline has not progressed at the pace envisioned and has proved to be better at raising additional capital than pushing its compounds through its pipeline at a consistent pace.

Company Overview:

Trevena, Inc. (NASDAQ: TRVN) is a biopharmaceutical company that discovers and develops biased ligands for the purpose of delivering the next generation of

medicines that target G protein-coupled receptors (GPCRs). "Ligand" comes from the Latin word, ligare, "to bind or tie." A ligand binds with a biomolecule, forming a complex connection that serves some biological purpose. A biased ligand displays functional selectivity, preferring some signal paths over others. TRVN's biased ligands target G protein coupled receptors.

Approximately 40% of all modern medicinal drugs target GPCR. The company became public in January of 2014 at \$6.50 a share, which is pretty much where it is currently trading even if its pipeline has made great progress since the company came public. The shares were north of \$12.00 a share as recently as late 2015. The stock has a market capitalization of approximately \$330 million.

Pipeline:

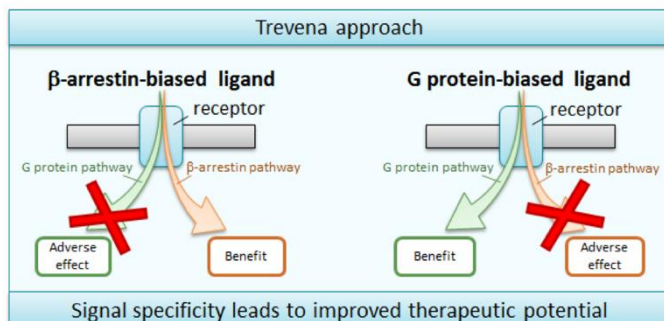
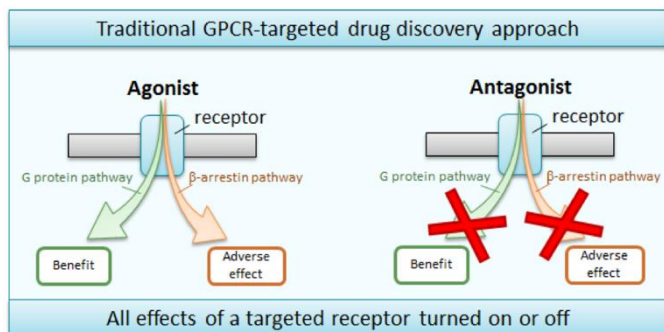
The company's proprietary platform has helped it quickly identify several drug candidates.

Here is a quick rundown of Trevena's current pipeline.

TRV130:

An intravenous treatment for moderate to severe acute pain. This compound was designed to optimize opioid receptor pharmacology using Trevena's ABLE™ platform and is intended to deliver an improved analgesic profile compared to conventional intravenous opioids. TRV230 is the first μ -receptor G protein pathway selective modulator, or " μ GPS", and is in development for the management of moderate-to-severe acute pain where intravenous therapy is preferred.

In November 2014, Trevena released positive top-line results from a Phase 2a/b study showing that a 3-mg dose of TRV130 had better analgesic (painkilling) effect than 4 mg of morphine. In February 2016, the FDA granted Breakthrough Therapy status to TRV130, also known as oliceridine. This designation is granted by the FDA to new therapies intended to treat serious conditions and for which preliminary clinical evidence



Biotech Gems

indicates that the drug may demonstrate substantial clinical improvement over available therapies. Top line data for two Phase III trials (APOLLO 1 & 2) using TRV130 should be disclosed before the end of the first quarter of next year.

TRV734:

Oral treatment for moderate to severe acute and chronic pain. TRV734 is an oral follow-on program to the intravenous TRV130 mu opioid biased ligand program. Like TRV130, TRV734 targets the mu opioid receptor, and selectively stimulates G protein coupling at the receptor, the mechanism by which opioid drugs confer analgesia. Successful Phase I studies suggested that TRV734 may be able to deliver better pain relief than current opioid analgesics like oxycodone, or equivalent pain relief to these drugs with improved safety and/or tolerability. Trevena is seeking a worldwide partner to develop and commercialize TRV734. Finding a partner could defray development costs and be a positive catalyst both for the stock and pipeline development.

TRV250:

In preclinical development for the treatment of refractory migraines. The acute episodic migraine market encompassed approximately 12 million drug-treated patients in 2013 in the United States, representing approximately \$2.2 billion of sales. Trevena estimates that approximately 20% to 30% of these patients either do not respond to, or cannot tolerate the market-leading triptan drug class, and an additional 30% would benefit from improved efficacy compared to these drugs. The Company expects to submit an investigational new drug application for TRV250 to the FDA by the end of 2016 which should be a nice positive when it occurs.

Addressable Markets:

While it is too early to estimate prices for these treatments should they eventually garner approval, it is easy to see that the addressable markets are enormous. This is another attribute we look for within our small

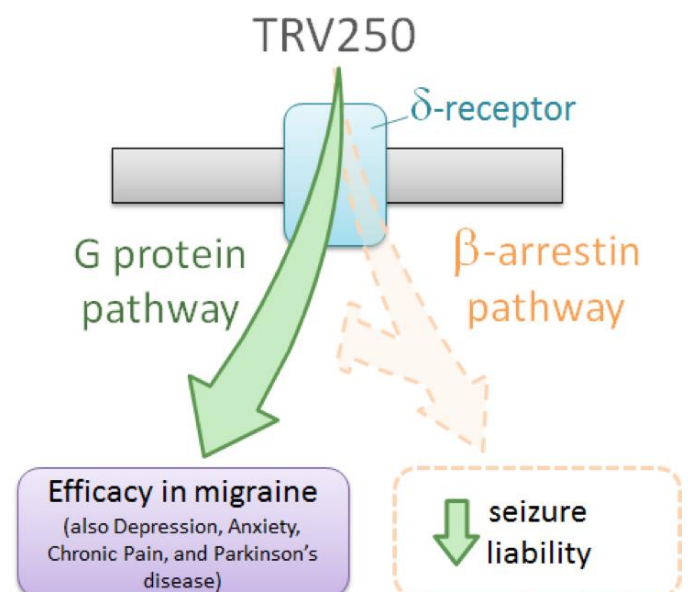
cap selections. It is very hard to develop any new compound so substantial existing demand is always a positive as success could mean a significant new drug.

TRV130: 20 million surgical procedures performed in 2013 resulted in reimbursement claims for injectable opioids for pain management.

TRV734: Opioid sales across the US, Europe and Japan amounted to \$11 billion in 2013.

Analyst Commentary and Balance Sheet:

The median price target on Trevena currently by analyst firms that cover the company is right near \$13.00 a share, or twice the stock's current level in the market. The company has also seen an acceleration of positive market commentary of late. Since late October, Aegis Capital, Needham, Roth Capital and Jefferies have all reiterated Buy ratings with price targets ranging from \$11 at both Needham and Jefferies to \$14.50 at Roth. The analyst at Roth was the last to chime in on Trevena on November 7 and is high on some upcoming catalysts "We continue to look for top line results from Trevena's APOLLO-1, and APOLLO-2 Phase 3 efficacy trials with oliceridine are expected in the first quarter of 2017. The APOLLO-1 trial is enrolling patients suffering moderate to severe pain after undergoing bunionectomy, while the APOLLO-2 trial is enrolling patients suffering



moderate to severe pain after undergoing abdominoplasty. Both trials are 375-patient, multi-center, randomized, double-blind, placebo- and active-controlled studies". At the end of the third quarter, the company had cash, cash equivalents, and marketable securities totaling approximately \$120 million which should take it well into 2018.

Outlook:

TRVN trades for \$6.50 a share, well below the average price target of \$13.00 a share as well as the highs reached late in 2015. The company has some \$120 million of cash on its balance sheet as of its last completed quarter which accounts for more than a third of its market capitalization. Raising additional capital is not an event that is on the horizon until at least 2018 as the company has sufficient funds to develop its evolving pipeline. The company should be able to file an NDA on TRV130, provided Phase III trials go well in the second half of 2017, which should be a major milestone for the company and the stock.

There has been some insider buying in Trevena in November. Two SVP's and officers, as well as the CEO, have bought stock totaling some \$90,000 so far in the month. This follows purchases of approximately \$150,000 by the CEO in late May.

I like the risk to reward profile of this small cap concern. Trevena has an interesting pipeline and a solid balance sheet. The stock could be buoyed by successful trial results or the announcement of a development partner for one or more of its current compounds in trials in the quarters ahead. Trevena also is getting increasingly nice mentions and support from analysts. Although like almost any small cap biotech company, it is speculative, it is promising enough to include in the Biotech Gems portfolio at approximately \$6.50 a share.

Recommendation: Buy Up to \$7.25 per share

Portfolio News

"Fame is a vapor, popularity an accident, and riches take wings. Only one thing endures and that is character." - Horace Greeley

Even with the slight pullback this week, it has been a very good month for investors in the biotech sector. The political backdrop has brightened considerably. Large caps are still selling collectively for some of their lowest valuations compared to the overall market in the last decade. In addition, I expect a significant pick up in M&A activity in the quarters ahead now that the market has political clarity, at least until the 2018 mid-terms. Drug and Biotech giants have large slugs of cash on their balance sheets, financing rates are still historically low and pipelines still need to be replenished.

If we get a good uptick in M&A deals, I expect the biotech sector to continue to rally and break through upward resistance levels that have been in place for most of 2016. I don't know if that will occur by yearend or in the first quarter. However, the outlook for the biotech sector is much more solid than it was just a few weeks ago.

Performance Update:

Our benchmark, the **iShares Nasdaq Biotechnology ETF (NASDAQ: IBB)**, the largest ETF focused on the biotech sector with almost \$9 billion in assets, is now down 17.23% since we launched the Biotech Gems service at the start of May of 2015.

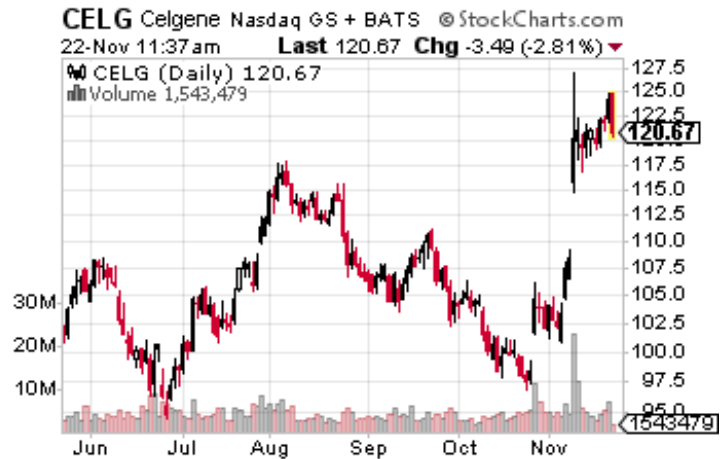
Our large cap core positions are down 6.69% on average while our small cap portion of our portfolio is now down 4.89% on average, both not including dividends. Using the minimum 50% allocation recommended to our core positions gives us a blended loss of 5.79%, 1,144 basis points above our benchmark. The most conservative allocation of 75% dedicated to the large cap core positions results in a loss of 6.24%, 1,099 basis points above the benchmark.

Portfolio News:

The portfolio beat its benchmark this week despite the latest disappointment around **Dynavax Technologies (NASDAQ: DVAX)** which plunged on the week after the FDA requested more data around its New Drug Application for HepLisav-B, its hepatitis B vaccine. This will push back any approval date. It is important to note the FDA is not requesting any additional studies and hasn't even been able to get through the data that Dynavax has already provided the agency. I added to my core stake on the sell-off. I am with William Blair on this one, that reissued a Buy rating while reducing the price target on DVAX to \$17 a share. This pushes back approval and will likely force Dynavax to find a development partner. However, the vaccine, based on study results, looks likely to be eventually approved. The company has other assets as well, including a promising oncology compound, "SD-101", and an asthma drug that is in Phase II development with partner, **AstraZeneca (NYSE: AZN)**.

On a much brighter note, **Tracon Pharmaceuticals (NASDAQ: TCON)** shot up some 30% this week from oversold levels. **Progenics Pharmaceuticals (NASDAQ: PGNX)** also continued its recent relentless run and is up 60% over the past few weeks. **Egalet (NASDAQ: EGLT)** and **Xencor (NASDAQ: XNCR)** also had another strong week.

Among our large caps, **Celgene (NASDAQ: CELG)** has gained over 15% since the election. I also expect we will get stronger performance out of some of our laggards like **Gilead Sciences (NASDAQ: GILD)** once tax loss selling season runs its course in a few weeks.



In this issue, we will be closing out our position in **Synthetic Biologics (NASDAQ: SYN)**. The pipeline is not developing as rapidly as I had thought and the shares no longer carry a high enough risk to reward.



Current Portfolio

Company	Entry Date	Entry Price	Recent Price	Buy Up To	Returns
Treva Inc. (TRVN)	11/21/16	\$6.48	\$6.48	\$7.25	N/A
Vascular Biogenics (VBLT)	10/17/16	\$4.95	\$4.90	\$6.00	-1.0%
Egalet Corporation (EGLT)	09/16/16	\$7.13	\$8.07	\$8.50	13.2%
Amicus Therapeutics (FOLD)	08/15/16	\$7.15	\$8.99	\$8.00	25.7%
Progenics Pharmaceuticals (PGNX)	07/07/16	\$5.44	\$8.25	\$6.25	51.7%
Supernus (SUPN)	06/13/16	\$18.70	\$22.25	\$21.50	19.0%
Artana Therapeutics (PETX)	05/12/16	\$5.49	\$7.79	\$12.00	41.9%
Ardelyx (ARDX)	04/20/16	\$8.05	\$15.40	\$9.50	91.3%
Celgene (CELG) - Core	03/31/16	\$100.09	\$124.16	\$110.00	24.0%
Merrimack Pharmaceuticals (MACK)	03/07/16	\$7.49	\$6.21	\$8.00	-17.1%
Eagle Pharmaceuticals (EGRX)	02/16/16	\$56.54	\$78.99	\$65.00	39.7%
TG Therapeutics (TGTX)	01/13/16	\$8.47	\$6.05	\$11.00	-28.6%
Xencor Inc. (XNCR)	10/07/15	\$12.49	\$26.80	\$15.00	114.6%
AbbVie (ABBV) - Core	09/28/15	\$52.50	\$60.42	\$62.50	15.1%
Lexicon Pharmaceuticals (LXRX)	08/24/15	\$11.33	\$16.47	\$12.50	45.4%
Mylan (MYL) - Core	08/10/15	\$57.52	\$36.68	\$60.00	-36.2%
TRACON Pharmaceuticals (TCON)	08/10/15	\$11.40	\$7.00	\$13.00	-38.6%
Amgen (AMGN) - Core	07/07/15	\$155.39	\$145.55	\$160.00	-6.3%
Synergy Pharmaceuticals (SGYP)	06/05/15	\$4.90	\$5.56	\$5.50	13.5%
Gilead Sciences (GILD) - Core	05/08/15	\$103.85	\$74.98	\$115.00	-27.8%

**Recent price is determined by the last "Close" price at the closing of the market on the day before publication; most recent update: 11/21/16.

Closed Positions

Company	Entry Date	Entry Price	Close Price	Returns	Close Date
Synthetic Biologics (SYN)	09/10/15	\$2.44	\$0.88	-63.9%	11/21/16
pSivida Corporation (PSDV)	06/22/15	\$4.03	\$2.28	-43.4%	10/17/16
Novavax (NVAX)	07/22/16	\$7.35	\$1.29	-82.4%	09/16/16
Inovio Pharmaceuticals (INO)	05/08/15	\$8.01	\$20.60	10.9%	08/15/16
Relypsa (RLYP)	11/13/15	\$18.96	\$32.07	69.1%	07/22/16
Celsion Corporation (CLSN)	07/21/15	\$2.45	\$1.30	-46.9%	07/07/16
XOMA Corporation	06/22/15	\$4.28	\$0.63	-85.3%	06/13/16
Pernix Therapeutics Holdings (PTX)	07/07/15	\$5.63	\$0.53	-90.6%	05/05/16
Pacific Biosciences of Calif. (PACB)	05/08/15	\$6.09	\$9.07	48.9%	04/20/16
Biogen Idec (BIIB)	10/23/15	\$276.99	\$260.32	-6.0%	03/31/16
Horizon Pharma (HZNP)	09/10/15	\$28.58	\$17.33	-39.4%	03/07/16
Heat Biologics (HTBX)	06/05/15	\$6.51	\$0.94	-85.6%	03/07/16
Protalix BioTherapeutics (PLX)	05/08/15	\$2.17	\$0.86	-60.4%	02/16/16

Notes:

Positions designated as “Core” represent the large-cap stocks in the portfolio that should make up 50% to 75% of an investors biotech portfolio depending on each subscriber's individual risk profile.

Entry price is determined by the last "Close" price at the closing of the market on the day before publication, which also serves as the Entry Date. Buy Up To is the upper share price limited recommended for buying new shares. Returns data is share price appreciation or depreciation between entry price and recent price.

This is not real-time data and should not be interpreted as such. All data is subject to change without notice.

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