

**RESEARCH REPORT ON
ARENA PHARMACEUTICALS
(NASDAQ: ARNA)
Price Target: \$100**

by

Arena Investor Group

Version 10 (29 OCT 2017)

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DISCLAIMER: The following material was put together as a collaborative effort between various Arena investors. Its purpose is to share why we believe that Nasdaq: ARNA currently presents a great investment opportunity for us. This report is not endorsed or sponsored by Arena (www.arenapharm.com). The estimations and calculations of price targets were done before the recent secondary offering. We made an effort to update these but there may be inaccuracies. We also attempted to update all stock price references to post-RSS units. **This report is not an investment advice. Please do your own research before making investment decisions.**

BIOTECH INVESTING

We like to invest in the biotechnology space because if you do the homework then the potential exists to identify a deeply undervalued company from which the stock price gains can be significant. We believe Arena (ARNA) fits the profile of a highly overlooked and undervalued company that could be on the verge of a breakout. ARNA has utilized proprietary science and a highly skilled workforce to ferret out a portfolio of potential best in class drugs that offer exciting potential.

Within the past year, a new management team has completely restructured the company, focused on developing the existing pipeline, put the finances in order and are executing according to plan. With positive data on multiple phase 2 trials in the coming months, we believe that a price target of \$100 completely possible by the end of the year (2017).

ARNA UNDERVALUED

JMP's Securities' Jason Butler called two of the pipeline assets "***potentially best in class***" and "***blockbuster***". JMP recently upgraded ARNA to *Market Outperform*. Jason Butler is a "5-star analyst".

Joseph Schwartz of Leerink Partners has recently initiated coverage of ARNA with price target of \$50). Mr. Schwartz is a star analyst with stellar ratings.

Piper Jaffray analyst Ted Tenthoff called Arena Pharmaceuticals the "***Turn Around Story of the Year: 3 Phase II Readouts in 2017***". Mr. Schwartz is also a star analysts with stellar ratings."

FBR & Co.'s Chris James (M.D., Managing Director of Equity Research-Biotechnology) initiated ARNA coverage with a buy rating and a price target of \$60. Recently another analyst at FBR (Rahul Jasuja) in a report reiterated their outperform rating and \$60 price target on shares of Arena Pharmaceuticals, Inc.

LifeSci Capital initiated coverage on Arena Pharmaceuticals on Aug 1, 2017 with a very detailed and positive 35 page research report that is available on this link:

www.baystreet.ca/articles/research_reports/lifesci/Arena080117.pdf

It is worthy to note that despite the positivity of the report that LifeSci Capital issued, they were apparently unaware that Arena already has one marketed product (Belviq) that it took from concept to preclinical through marketing authorization. A deal was struck with Eisai only for commercialization once formal approval was near. The public awareness of Belviq is sure to change with the upcoming release of data from the 5 year, 12,000 patient cardiovascular outcomes (CVOT) trial now being run by Eisai. These results are expected sometime in 2H 2018. Although sales of Belviq have been disappointing thus far, if CVOT data reveals (as we expect) that Belviq is not only the safest available weight loss drug as well as an effective agent against type 2 diabetes, the sales of Belviq are likely to begin taking off in 2H 2018. Arena's introduction of the extended

release version of Belviq (Belviq XR) about a year ago is sure to make the case for Belviq even more compelling.

Below we explain our logic for believing that these target price estimates are very conservative and with good data coming in, we expect revised, higher target prices.

ABOUT ARENA (Nasdaq: ARNA)

Arena discovers and develops medicines for serious diseases with a philosophy of developing highly specific drugs targeting high-impact and underserved areas of medical need. The core and novel GPCR drug discovery engine developed by Arena scientists allows for highly selective targeting of GPCRs and these efforts have produced numerous compounds with potential “best in class” characteristics.

G-Protein Coupled Receptors (GPCRs) are the most important family of receptors researched by the drug industry with some 40% of all modern medicines targeting GPCRs.

ARENA has a proprietary approach to targeting GPCRs along with the synthesis and selection/fine-tuning of highly selective GPCR modulators. Selectivity means that ARNA’s drugs avoid closely related receptors thus avoiding unwanted off-target effects. Avoiding activity against other receptors can result in a huge benefit in terms of minimizing side effect profiles in patients. ARNA maintains a strong patent portfolio on their compounds.

So, exquisite specificity and safety in design are some of Arena’s key competitive advantages in the area of GPCR drug discovery and development. Keep in mind that sometimes it is useful to activate (agonize) instead of inhibit a particular drug target. ARNA’s drug discovery engine (now with private spin-off company Beacon Discovery) is just as capable of developing GPCR activators (i.e. agonists) as inhibitors (antagonists and inverse agonists) as the science dictates in order to address the therapeutic goals of the disease target involved.

ARNA PAST & PRESENT

Arena’s proprietary technology has produced five potentially “best in class” compounds that are currently in mid-stage clinical trials (Etrasimod, Ralinepag, Nelotanserin, APD371) or already on the market (Belviq).

- Class leading specificity and safety means extending utility (and profit) beyond what is possible for competitor compounds in the same categories.

The Evolution of ARENA Over the Last 14 Months

- Prior to May 2016, Arena spent a long time and lots of money developing a best-in-class obesity and Type 2 Diabetes (T2DM) medicine lorcaserin (Belviq) which has a very clean safety profile. Although safe and effective, sales have been sluggish. Although Belviq may yet become a blockbuster (see below), the rest of the Arena’s pipeline languished. Historically, ARNA suffered from a number of bad management decisions along with slow uptake of Belviq by the obesity community. In 2016 ARNA’s CEO Jack Lief was finally asked to step down and a major remodeling of management ensued.
- Beginning in May 2016 a new CEO (Amit Munshi) was hired and since then the Management Team has been dramatically re-engineered and refocused on fully extracting the tremendous value present in ARNA’s mid-stage pipeline. The company has been:

- Right-sized with enough cash to carry the company into mid- to late-2018 (multiple phase 2 programs on 3 wholly owned assets report results prior to that time and one or more partner deals is expected before then.)
- Rebuilt with significantly expanded clinical development functions
- Restructured in non-core areas
 - Spun-off the costly Discovery unit into the private “Beacon Discovery” organization while retaining key intellectual property rights on current assets
 - Restructured their partnership with Eisai to offload all future costs of Belviq development and marketing while retaining a healthy tiered royalty (9.5% - 18.5%) on all future Belviq sales
- New focus in on clinical development of 3 wholly owned assets:
 - **Etrasimod**- a potential best in class and wholly owned SIP1 receptor modulator to treat a wide range and rapidly expanding range of inflammatory conditions.
 - Celgene recently paid \$7.2 billion for a similar compound with unwanted side effects that Etrasimod does not have.
 - **Ralinepag**- a potential best in class and wholly owned prostacyclin agonist (with Orphan Drug status!) for the treatment of a potentially fatal condition (Pulmonary Arterial Hypertension). Notably, ralinepag also represents the first oral PAH medication with intravenous-like dosing qualities.
 - Potential sales are currently estimated at \$1.5 billion a year for J & J’s Upravi (selexipag), (which appears to be an inferior competitor compound to Ralinepag based upon currently available phase I safety and specificity data)
 - Drugs with an Orphan Drug Status have higher approval rates than those that do not.
 - **APD371** – a potential best in class and wholly owned novel cannabinoid CB2 full agonist (almost all competitor compounds are only partial agonists with significant off-target activity). Why is full agonist activity vs. the CB2 receptor important?
 - Full agonist activity against CB2 appears to be necessary for effective pain relief (full agonism prevents receptor silencing or tachyphylaxis).
 - APD371 also has activity that could make it an effective anti-inflammatory!
 - APD371 was designed to avoid getting into the central nervous system (i.e. it cannot effectively pass through the blood-brain barrier) and thus there are no worries about psychotropic or behavior effects when taking APD371!

CLINICAL TRIAL UPDATES

Ralinepag Phase 2 Trial Results – The more we look the better it looks!

October 2017, based on [http://journal.chestnet.org/article/S0012-3692\(17\)32286-9/fulltext](http://journal.chestnet.org/article/S0012-3692(17)32286-9/fulltext)

Ralinepag significantly improved PVR compared with placebo in subjects with FC II-IV PAH on single or dual background therapy, and showed excellent safety, and better safety than Selexipag. Serious adverse events (AEs) occurred in 10% of ralinepag subjects and 28.6% of placebo subjects.

The Selexipag phase 2 group experienced 18.2% serious adverse events. Ralinepag improvement of 36.2 M is better than Selexipag's that showed 24.2 M in the similar phase 2 trial.

Reminder: Selexipag obtained a valuation of around \$8B for Actelion when Johnson & Johnson bought them for over \$30 Billion.

\$8B in Arena terms translates to \$200/ shares. ARNA is currently trading under \$30, and has several other hot pipeline items, including Etrasimod which seems to be better and safer than Ozanimod (Phase 2 data is expected by end of the year as reiterated numerous times by management), and APD371, a non-addictive, non-psychotropic compound for pain and other conditions. Data on APD371 is also expected by year-end 2017.

Ralinepag Phase 2 Trial Results – Success! (July 10, 2017)

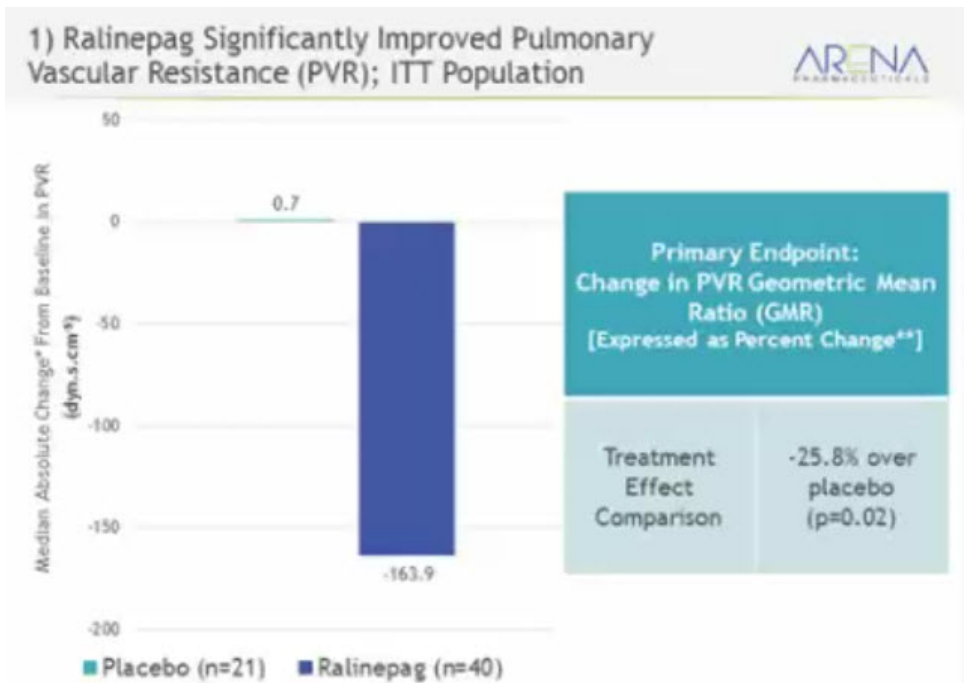
“These Phase 2 results are extremely compelling, particularly considering the contemporary patient population of our trial in which 65% of patients were already receiving dual background therapies and all patients were receiving at least one therapy,”
Preston Klassen, MD, MHS, executive vice president, Research and Development and chief medical officer of Arena, said.

See **Ralinepag potentially Best in Class & better than Selexipag; Arena Pharmaceuticals (Nasdaq:ARNA)** : <https://www.youtube.com/watch?v=QOVAgg6OcpA>

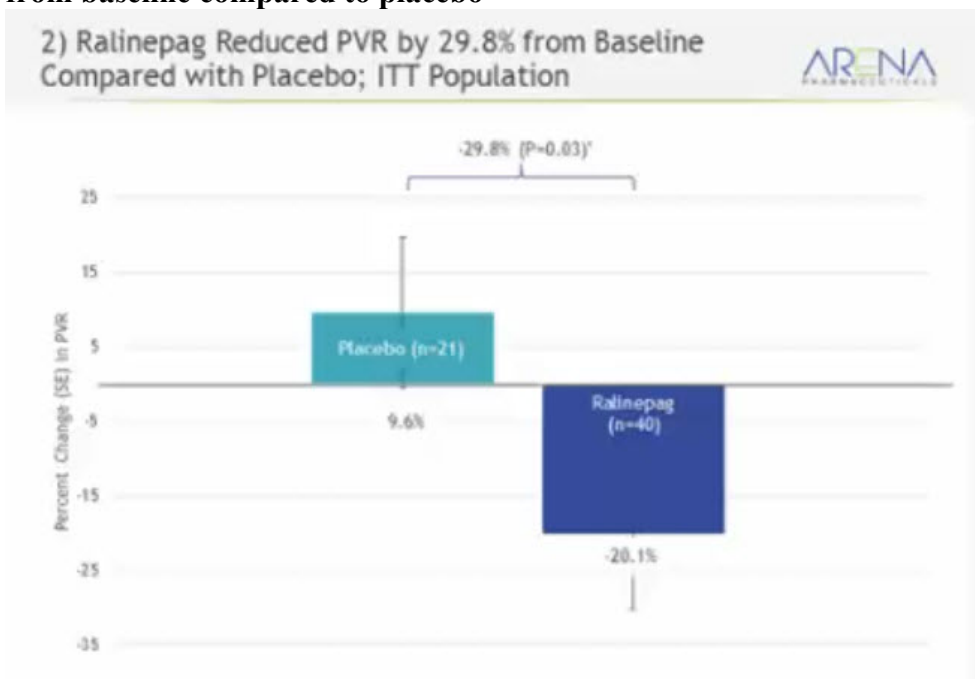
Dr. Preston Klassen (Chief Medical Office of Arena Pharma) announced on July 10, 2017 the stellar results of the long anticipated Phase 2, proof of concept trial for Ralinepag. The trial consisted of 61 patients with 40 in the Ralinepag group and 21 in the placebo group. Baseline PVR (Pulmonary Vascular Resistance) was higher in the Ralinepag group (median PVR numbers (705R vs. 480P). Mean 6 minute walk distance was 351 meters in the placebo group and 393 meters in the R group (a difference of 30 meters in this test is considered medically significant). There were no treatment naïve patients in either placebo or ralinepag groups. All patients were on background therapy with mono- or dual therapy in addition to placebo or Ralinepag, highlighting the cautionary approach to trial design for these very sick patients. Placebo and ralinepag groups were also similar in that about the same percentage of patients in each group were either WHO (World Health Organization) functional classes II or III (so patients between the P and R groups could be considered equally encumbered by their disease). An important point made by Dr. Klassen was that because the Ralinepag group was more heavily background-treated with dual therapy than the placebo group (65% vs. 48%) that the positive effects of Ralinepag might be more difficult to see. Over a 9 week dosing titration period, almost 60% of patients achieved the highest doses of Ralinepag. This is significant because it shows that PAH patients can tolerate the higher doses of Ralinepag (200, 400, and 600 ug/day) and this is expected to equate with a higher therapeutic benefit and thus become more like the gold standard IV like therapy for patients. Here are the detailed results of the study:

1) Primary efficacy analysis – change in PVR (Pulmonary Vascular Resistance)

- PVR in the Ralinepag group dropped by 25.8% vs placebo (p value = 0.02)
(this result means Ralinepag met its primary endpoint for efficacy making this a positive, successful proof of concept study)



2) Ralinepag also met its secondary endpoint by reducing PVR by a substantial 29.8% from baseline compared to placebo



Physicians generally consider a PVR drop from baseline of 15% to 20% as clinically important. Ralinepag dropped the PVR from baseline a solid 20%, at the top end of this range (and also provided a 30% improvement compared to placebo)

3) Ralinepag also met its tertiary endpoint by increasing the 6 minute walk distance by 36.2 meters from baseline (statistically significant at $p = 0.003$). Physicians generally consider anything around the 30 meter mark as clinically meaningful. The placebo group by comparison increased the 6 minute walk distance by just under 30 meters but the result in the placebo group had large error bars so the result was not considered statistically

significant (it is also important to keep in mind that 2 patients in the placebo group died during the course of the trial, 0 deaths in the Ralinepag group).

(Other findings: serious adverse events occurred in 10% of patients taking Ralinepag vs. 28.6% of patients taking placebo)

Summary

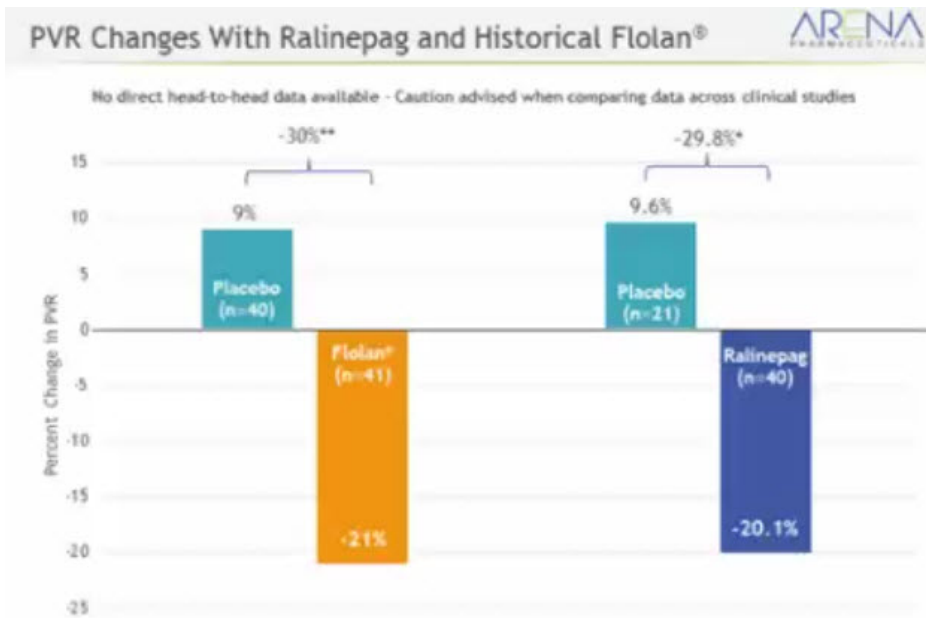


Successful Phase 2 Trial Results Inform Progression to Phase 3 Program

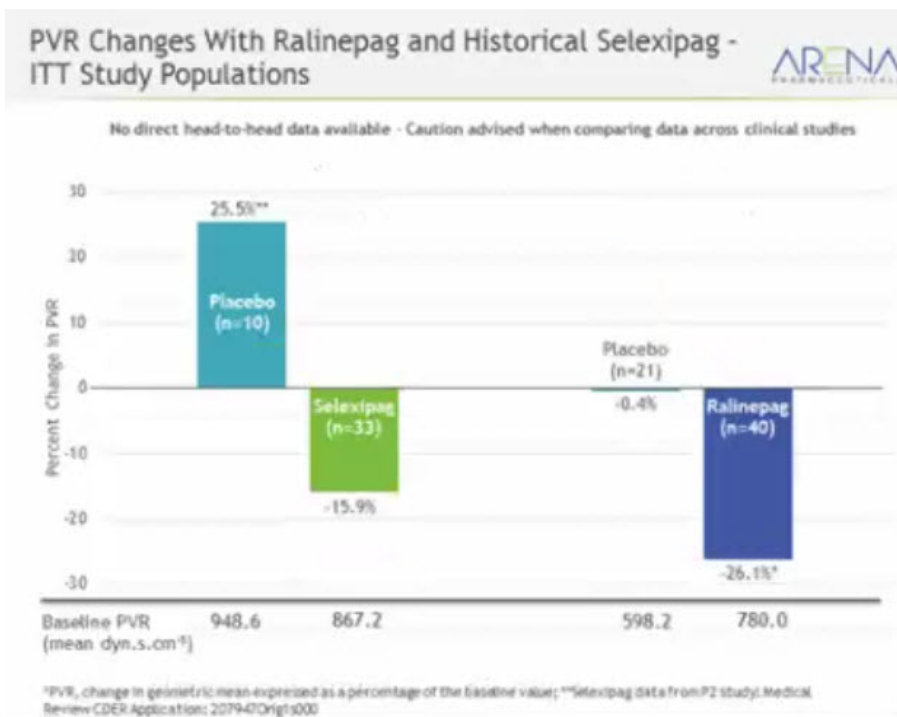
- Ralinepag Phase 2 trial results demonstrate meaningful efficacy among a contemporary PAH population
 - Majority of patients receiving background dual combination therapy
 - Ralinepag reduced median PVR by 163.9 dyn·s·cm⁻⁵ from a baseline of 705 dyn·s·cm⁻⁵
 - Statistically significant improvement over placebo for both absolute change (geometric mean ratio) and percent change
 - Clinically meaningful numerical improvement in 6MWD
- Tolerability and adverse event profile consistent with the known effects of therapeutics in the prostacyclin class
 - Dose titration tolerated as expected
 - No increase in serious adverse events or death compared to placebo
- Phase 3 planning underway

Additional Important Points to Consider for the Future of Ralinepag:

- 1) This trial was conducted in a contemporary population of background treated PAH patients, the majority of which were already receiving dual therapy with other agents.
- 2) PVR Results with Ralinepag were consistent with what has been seen for the current gold standard of treatment for PAH (continuous IV infusion)



3) Comparison to Selexipag PVR results



- In the Selexipag trial only 30% of patients were on dual background therapy vs. 65% in the Ralinepag group. This actually makes it more difficult to see a positive comparative result for Ralinepag vs. placebo (i.e. dual therapy more likely to mask a positive result).

4) These very encouraging phase 2 results detailed above suggest that Ralinepag will take an important place in the future of therapies available to the patients suffering from PAH

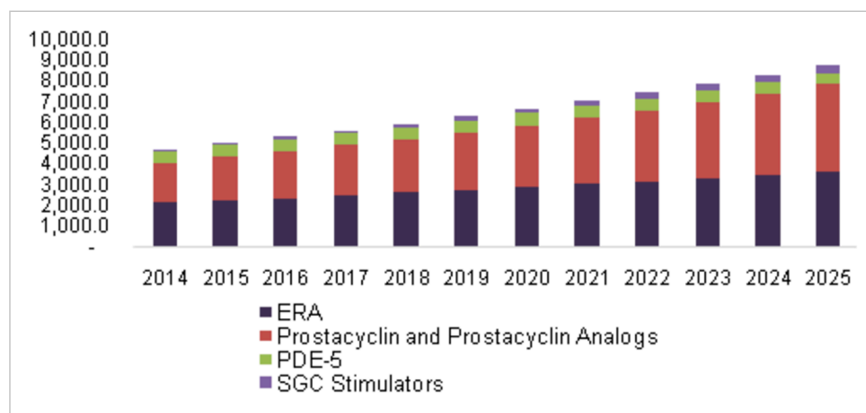
The oral prostacyclins continue to be the dominant class of drugs used to treat PAH

- The PAH market is expected to reach \$7-8 billion by 2025 with the greatest portion of that coming from the oral prostacyclin agonists.
- Key takeaways from a PAH key opinion leader conference that took place on May 25, 2017 are as follows:
 - No therapeutics available or in development are likely to ever replace oral prostacyclin receptor drugs as a key treatment for PAH
 - Currently available evidence points to Ralinepag as best in class
 - Update July 2017: Ralinepag XR data in phase I trials indicate that Ralinepag can now be dosed in a once a day formulation (more like continuous IV infusion) that increases effective exposure while reducing side effects that may result from spikes in plasma levels of drug that are seen with multiple dosing regimens using immediate-release formulations.
 - Link to the conference: <http://lifesci.rampard.com/20170525/reg.jsp>
- Ralinepag competitor Selexipag, the current cornerstone compound in the oral prostacyclin class, was recently purchased from Actelion by Johnson and Johnson (this was a \$30 billion deal with Selexipag (Uptravi) playing a major role in the purchase price).
- Selexipag (Uptravi) is a weak partial agonist and yet is expected to garner a yearly revenue in the 1-2 billion dollar range.
- So, how does Ralinepag compare to Selexipag?
 - Ralinepag is a strong partial agonist vs. the weak partial agonism of Selexipag
 - Ralinepag is 6.5x to 10x more active than Selexipag in prostacyclin pathway readouts
 - Ralinepag is more efficacious than Selexipag in assays of small pulmonary artery relaxation (vasodilation) and in the inhibition of smooth muscle cell proliferation and platelet aggregation (by these criteria. Thus, Ralinepag is more likely to offer more therapeutic relief and inhibit pathological progression of PAH better than Selexipag.
 - In measure of smooth muscle cell proliferation (one of the pathological hallmarks of PAH) Ralinepag is roughly 10x more efficacious than Selexipag. Note: these assays were conducted in blood vessels taken from PAH patients!
 - In measures of inhibition of platelet aggregation, Ralinepag is roughly 6.5 x more efficacious than Selexipag
 - Ralinepag has vastly superior and continuous intravenous like infusion pharmacokinetics (how the drug gets into and stays within therapeutic range after dosing) than Selexipag
 - Preclinical data has already shown a reduction on right ventricular hypertrophy in animal models of PAH. In light of the recent phase 2 data with Ralinepag, it is likely that this result will transfer to humans as well.
 - If all the above isn't impressive enough, note that a once a day formulation Ralinepag-XR is expected to be used in the upcoming phase 3 trial.
- How to compare upcoming results in the phase 2 trial results of Selexipag with the upcoming results for Ralinepag?
 - An apparently widely misunderstood perception about the Selexipag phase 2 trial is that it compared Selexipag alone against placebo without any background medications involved. An excerpt from a publication describing

the results of this trial (Eur Respir J 2012; 40:874-880) clearly states: “43 adult patients with symptomatic PAH (receiving stable endothelin receptor antagonist and/or a phosphodiesterase type-5 inhibitor therapy) were randomized three to one to receive either selexipag or placebo. Dosage was up-titrated in 200-mg increments from 200 mg twice daily on day 1 to the maximum tolerated dose by day 35 (maximum allowed dose of 800 mg twice daily)”.

- Since it appears that the placebo group in the Selexipag trial received more often one and not both of the background medications as the Selexipag arm {“treatment groups were balanced with respect to demographics and aetiologies (table 1) and patients were on stable background PAH therapy (table 2). In the PP set, 11 (37.9%) patients in the selexipag group were on a combination of ERA and sildenafil therapy versus one (16.7%) patient in the placebo group”} this may have skewed the results to make Selexipag outcomes look more favorable than they really were. As it turns out, the placebo group in the Selexipag phase 2 trial did get worse over time.
 - To compare Selexipag and Ralinepag results will require a careful understanding of how the background treatments and severity of illness compares between the trials. It may be that a head to head comparison may be necessary to completely answer this question.
- PAH is a life-threatening condition and many drug companies are racing to develop more effective and more convenient therapies. Recent failures of competitor compounds (see below) highlights the recognized need for better therapies to treat PAH and we believe with its excellent specificity and safety profile that Ralinepag has the best shot yet to improve the lives of patients suffering from this debilitating and deadly condition
- The PAH market is currently around \$5 billion a year and there is a crying need for an improvement over the current standard of care. Ralinepag has orphan status with all the benefits that entails.
- The competition: <http://www.nasdaq.com/article/gilead-says-phase-2-study-of-gs4997-in-pah-did-not-achieve-primary-endpoint-20161020-00796>

Pulmonary Arterial Hypertension market, by drug class, 2014 - 2025 (USD Million)



Etrasimod

Etrasimod – an oral, next generation S1P1 receptor modulator is currently being evaluated for multiple autoimmune conditions

- First generation compounds (unlike etrasimod) tended to be pan S1P receptor (S1P1, S1P2, S1P3, S1P4, S1P5) modulators that target either all or additional problematic S1P receptors
 - Celgene's Ozanimod (purchased from Receptos for about 7.2 billion dollars) although a next-generation compound, has troubling off-target activity against S1P2 which could be problematic for some patients.
 - Etrasimod shows strong specificity for S1P1 (present on T cells) but also some additional and wanted specificity for S1P4 (present on dendritic cells) and S1P5 (present on multiple cell types with immune activity) but no relevant activity against side-effect causing S1P2 and S1P3 activities. The additional activity that Etrasimod has against S1P4 and S1P5 is considered favorable as S1P4 activity in dendritic cells is expected to inhibit inflammatory activity in these cells and S1P5 activity is expected to be beneficial in autoimmune conditions of the Central Nervous System (such as multiple sclerosis).
 - Oct 2017: CELG is now scrambling, after the failure of Mongersen (GED-0301), to begin Ozanimod trials in Crohn's. It may be that ARNA will not be too far behind CELG in getting a phase 3 clinical trial started for Etrasimod in Crohn's.
 - Oct 2017: CELG down due to failure of their new Crohn's drug GED-301 and overall weak guidance. Their renewed focus on using Ozanimod in the IBD and Crohn's disease is indeed good news for ARNA because some believed that Crohn's was not as good a target for S1P1 drugs as is multiple sclerosis. CELG's new focus on Crohn's with Ozanimod suggests otherwise.
- Etrasimod is currently in a phase 2 clinical trials for:
 - Ulcerative Colitis is the primary study with data readout expect in late 2017
 - Extra-intestinal manifestations of inflammatory bowel disease (IBD) including Crohn's disease (S1P4 activity relevant here)
 - Pyoderma gangrenosum, an inflammation-based skin condition
 - Etrasimod's activity against dendritic cells (S1P4) and keratinocytes appears relevant to expectations for a successful outcome in these PG trials...readout expected late 2017
 - Primary biliary cholangitis (PBC) trial is expected to start later this year
- Etrasimod has already demonstrated robust and reversible lymphocyte reduction in Phase 1 clinical trials. Lymphocyte reduction can be considered a leading indicator of clinical efficacy
- In contrast to Ozanimod and other competitor compounds, Etrasimod demonstrates no first dose cardiac side effects and does not need to be carefully titrated in patients. Also importantly, Etrasimod use is not associated with any changes in liver, lung or eye function (macular edema)
- Based upon all of the above, Etrasimod appears to be emerging as a potential best in class S1P1 modulator
- If you investigate the science and the trial results of Celgene's Ozanimod you will realize that the drop in serum lymphocyte counts observed in early trials of that drug were a strong surrogate for proof of concept. In phase 1 trials Etrasimod has already demonstrated similar drops in blood lymphocyte counts that have spelled success for Ozanimod (and with fewer side effects!). Celgene expects Ozanimod sales to be in the range of 2.5 to 6 billion dollars per year. APD 334 is only 8 months away from further confirmation of its lymphocyte

lowering capabilities and safety profile (as observed in its phase 1 trials) and should will earn a significant share of that market after approval if efficacy is demonstrated as expected.

- A recent review of S1P modulators was published and is available free for download from the Arena website: <http://www.arenapharm.com/category/publications/etrasimod/> The following figure and table from that publication helps us understand the potential value of Etrasimod in treating inflammatory conditions (and why avoidance of activity against S1P2 and S1P3 is important as well).

L. Peyrin-Biroulet et al. / Autoimmunity Reviews 16 (2017) 495–503

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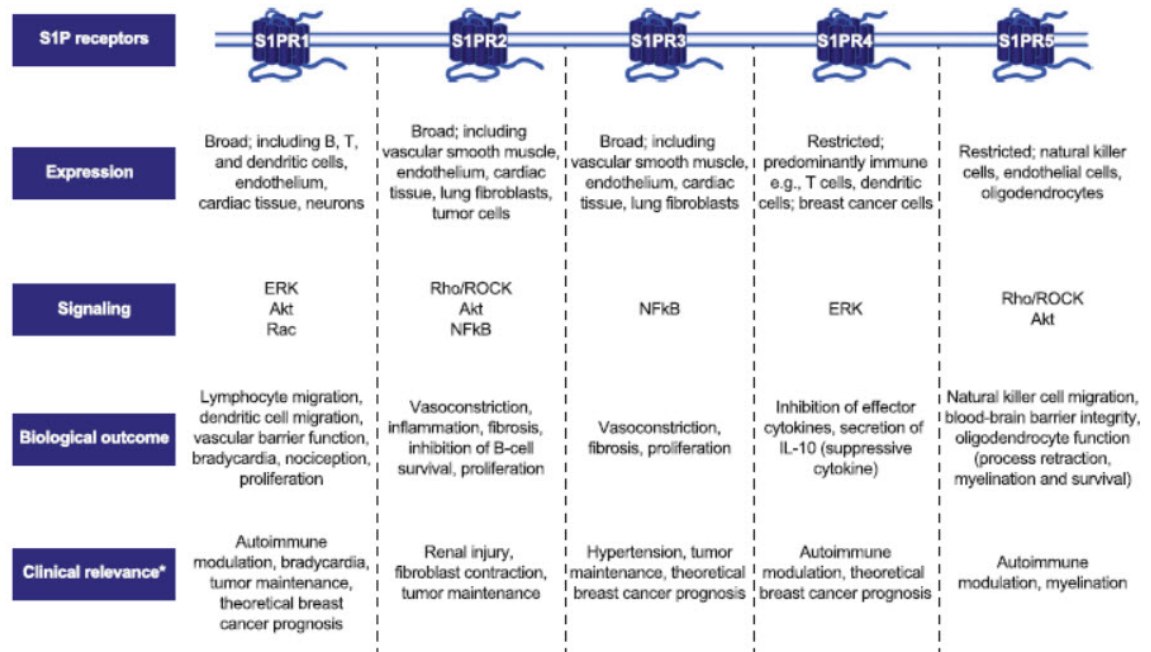


Fig. 1. Expression, downstream signaling molecules and function of S1P receptor subtypes [13,15–24]. ERK, extra cellular signal-regulated kinase; IL-10, interleukin-10; S1P, sphingosine-1-phosphate. *Based on a combination of animal and human data.

Table 1

Affinity of S1P and S1P modulators for human S1P receptor subtypes [14]. pEC₅₀, the negative logarithm to base 10 of the half maximum effective concentration of an agonist.

pEC ₅₀	S1P1	S1P2	S1P3	S1P4	S1P5
S1P	7.1–9.4	8.1–8.5	8.4–9.8	7.2–8.1	7.4–8.9
Fingolimod-phosphate	8.1–9.5	7.5	7.8–9.4	6.6–9.2	8.2–9.5
Ozanimod (RPC1063)	9.8	No response ^a	No response ^a	No response ^a	7.3
Etrasimod (APD334) ^b	6.10	No response	No response	147	24.4

S1P, sphingosine-1-phosphate; NR, not reported by Spiegel 2016; no published data available.

^a NR, not reported by Spiegel 2016; no response was based on *in vitro* potency and selectivity preclinical studies of human S1P receptor subtypes in various assays [51].

^b Data reported in preclinical studies on recombinant human receptor subtypes in a β-arrestin assay [52].

APD371

APD371 – A highly specific and potential best in class full agonist of the cannabinoid 2 receptor (CB2) currently in a phase 2 trial to treat visceral pain associated with Crohn’s disease (readout expected before the end of 2017). Although not often discussed, approximately 20% of all inflammatory bowel disease patients have persistent symptoms and pain associated with their condition that results in 1 of 6 patients requiring treatment with opioids for pain relief. Obviously, opiates, as well as other pain relief products on the market, have a range of undesirable side effects.

- Current competitor compounds that have failed or are in development in the cannabinoid area appear to lack the specificity (i.e. they may be considered to be pan-cannabinoid agonists) and the full CB2 agonism of APD371 and thus these other compounds are expected to have only marginal efficacy against pain.
 - APD371 has 10,000-fold specificity for CB2 vs. CB1
- Unlike other competitor compounds, APD371 is unable to pass through the blood-brain barrier (i.e. no entrance into the central nervous system) and thus APD371 is not expected to have any behavioral or psychotropic effects in patients (certainly these were not evident in completed phase 1 clinical studies with APD371). This fact will be welcomed by the medical community as avoiding behavioral effects makes the argument that APD371 could be an effective opiate replacement even more compelling.
- In preclinical trials, APD371 showed morphine-like efficacy with no psychotropic or addictive side effects! If the upcoming phase 2 trial results (currently slated to be reported by the end of this year) are as positive as animal studies suggest, ARNA’s share price could swing dramatically to the upside.
- CB2 receptors are expressed throughout the GI tract in tissues and in visceral nerves known to be conductors of pain sensations. CB2 receptors are expressed throughout the enteric nervous system (the mass (size) of the entire enteric nervous system is quite large and is often spoken of as “our second brain”)
- CB2 receptors are over expressed in inflammatory conditions in the gut
- There is a very strong scientific rationale for CB2 involvement in gut pain with both inflammatory and non-inflammatory components
- ARENAs pre-clinical research has already shown that the visceral endocannabinoid (EC) system is very important in the regulation of intestinal pain and that CB2 activation can alleviate abdominal pain. Additional facts to consider:
 - The endocannabinoid system is highly dysregulated in Crohn’s disease
 - In preclinical studies, APD371 is as effective against pain in rodents as opioids!
- In summary, the combination of a strong biologic rationale and preclinical investigations suggest that ARNA is heading down the right path with APD371
- Future plans for APD371 include a range of other visceral conditions which may include irritable bowel syndrome (pain associated with IBS), endometriosis, cholecystitis, chronic prostatitis and others
- The potential market size for APD371 and visceral pain is obviously quite large
- A main problem with most CB2 drugs is they also have activity against the CB1 receptor, resulting in unwanted side-effects. Discussions with a former research scientist from MRK who specialized in this area and reviewed several drugs for potential partnering, indicated that if the CB2/CB1 ratio was 10:1 or better that would be a definite plus for the compound. ARNA’s data so far shows that APD371 has a 1000 to 1 targeting specificity for CB2 over CB1!

Although very impressive, the above represents only part of ARNA's future potential...this is because ARNA already has two other compounds (Belviq and Nelotanserin) worth mentioning. ARNA, through its private partner Beacon Discovery, also has significant interests and rights in a research partnership with Boehringer Ingelheim (<http://www.prnewswire.com/news-releases/boehringer-ingelheim-and-arena-pharmaceuticals-collaborate-to-advance-research-in-schizophrenia-300203151.html>).

Oct 2017: Pipeline Therapeutics is a San Diego-based biotechnology company backed by Versant Ventures, with a focus on neurodegenerative diseases. As they assemble a world-class research team, Pipeline will work with Beacon on assay development and high-throughput screening (HTS) for an orphan GPCR target. In addition, Beacon will assist with a more advanced project where our expertise in a wide range of receptor binding and functional assays should accelerate the launch of Pipeline's discovery programs in this important disease area. You can find out more about Pipeline at their website: www.pipelinetherapeutics.com

Any compounds Beacon develops, Arena will have specific rights options. Arena will work with Beacon to support Arena's pipeline programs, as well as its collaboration with Boehringer Ingelheim International GmbH. That collaboration was announced in January of 2016. The two companies have an exclusive agreement to perform joint research to identify drugs that target an undisclosed GPCR that belongs to a family of orphan central nervous system (CNS) receptors. Arena is eligible for up to \$262 million in milestones payments from Boehringer, as well as possible tiered royalties.

PARTNERED PROGRAMS

Nelotanserin

Nelotanserin— is a potential best in class 5HT_{2A} inverse agonist that was licensed to Axovant (AXON) contingent upon a 15% downstream royalty to ARNA (additional developmental and regulatory milestones in the \$40 million dollar range are also included in the deal with AXON).

From the AXON website: Nelotanserin is an investigational drug candidate that has the potential to be a best-in-class, once-daily, orally-administered, potent and highly selective inverse agonist of the 5HT_{2A} receptor. The 5HT_{2A} receptor has been linked to neuropsychiatric disturbances including visual hallucinations – a common occurrence in people living with Lewy Body Dementia. Axovant intends to develop nelotanserin to address multiple aspects of Lewy Body Dementia. In a release of preliminary phase 2 results with Nelotanserin in Lewy Body Dementia (LBD) AXON noted the following: The mean change from baseline in the UPDRS Parts II + III (this includes motor skills!!) exhibited statistically significant improvements (p-value < 0.05) for Nelotanserin relative to placebo. This result is consistent across least squares and observed mean changes. In addition to results from more comprehensive phase 2 studies with Nelotanserin, a phase 3 clinical trial with Nelotanserin is expected to start before the end of this year.

Nelotanserin is a potential best in class compound (again) competing with recently approved antipsychotic medicine Pimavanserin (Nuplazid, ACAD). Nelotanserin is a potential “best in class” in modulating the 5HT_{2a} receptor (Nuplazid has side effects because it also hits the 5HT_{2c} receptor). Nuplazid is the only drug in the pipeline of ACAD. Nelotanserin now being targeted by AXON for the same indications as Nuplazid. The market potential is again quite large.

To learn more about how Nelotanserin works watch this short video:

<http://axovant.com/wp-content/uploads/video/AxovantNelotanserinV8.mp4>

Nuplazid is the only drug in the pipeline of ACAD and ACAD's valuation is almost \$ 5 billion. The latest Nelotanserin results were excellent ($p < 0.05$ achieved for primary endpoint despite very small sample size) and we anticipate the full results will even be better. Bring Nelotanserin down to Arena's royalty level and downgrade it to Phase 2 and Arena's valuation on just Nelotanserin should be around \$750 million (currently assessed at zero). Nelotanserin phase 2 results later this year could add around \$23 a share to ARNA.

On June 7, 2017 Axovant Sciences gave a corporate update and shared some data slides (from data obtain in Feb. 2017) about the effectiveness of Nelotanserin in LBD (see below). Axovant made it clear that LBD is being targeted as the “first” indication because of the large (over 1 million in the U.S.) patient population. This is a much bigger indication than Multiple Sclerosis for example. It was clear from the presentation that Axovant is now confident enough in its data to indicate that they are now pursuing 3 (and not 2 as before) indications in Lewy Body Dementia:

- 1) Visual hallucinations
- 2) Motor Symptoms
- 3) REM Sleep behavior disorder

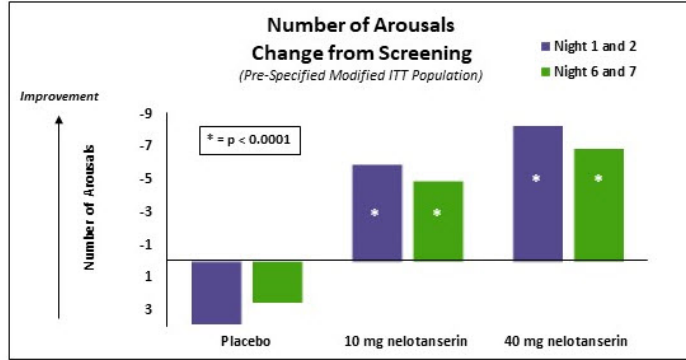
Axovant has been able to enroll more patients in these open label studies (which read out in the 2nd half of 2017) than initially indicated. The REM sleep behavior study is also being conducted in a sleep laboratory setting according to “gold standards” and Axon is positioning itself so that it may be able to submit the sleep study (~50 patients currently enrolled) results as a registrational trial (that means the possibility of filing for approval for the sleep disorder after completion of the phase 2 sleep study). The data obtained by Arena (below) has Axovant very hopeful about the sleep results to come from its phase 2 study. The second slide pasted below (on motor function improvement) shows data collected and analyzed earlier in this year (Feb 2017). The immediately following slide is from a sleep study conducted by Arena Pharm on “nelotanserin” prior to licensing it to Roivant/Axovant Sciences.

NELOTANSERIN: REM SLEEP BEHAVIOR DISORDER

NELOTANSERIN PHASE 2 STUDY DEMONSTRATED STATISTICALLY SIGNIFICANT IMPROVEMENT IN NUMBER OF AROUSALS FROM SLEEP

Nelotanserin Phase 2 Objective Sleep Study

- n = 173 adult subjects with primary insomnia
- Nelotanserin showed statistically significant benefits on wake time after sleep onset, the primary endpoint



Axovant Sciences Corporate Presentation – June 2017 For Investor Use Only

Sources: Rosenberg et al., SLEEP 2008; McKeith et al., Neuropsychopharmacology 2002.

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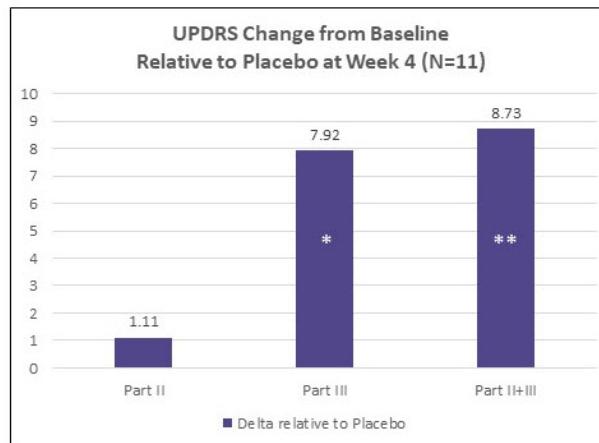


NELOTANSERIN OVERVIEW: MOTOR FUNCTION

PRELIMINARY DATA SUGGEST NELOTANSERIN MAY IMPROVE MOTOR FUNCTION AS MEASURED BY UPDRS

11 subjects with either DLB or PDD completed treatment in both 4-week crossover periods

Axovant plans to expand patient recruitment to confirm the treatment benefits observed in this study



* p-value = 0.005 ** p-value = 0.012

Axovant Sciences Corporate Presentation – June 2017 For Investor Use Only

UPDRS Part II measures activities of daily living
UPDRS Part III measures motor function

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The improvement in motor function is extremely promising in the LBD patients because the latter stages of disease are often associated with Parkinsonism movement disorders and the standard therapy for this condition in LBD patients is to add dopamine to the protocol. It turns out that

giving dopamine to LBD patients with Parkinsonism worsens the neuropsychiatric symptoms in these patients. The ability of Nelotanserin to improve the movement disorders inherent in latter stage LBD signals a new opportunity to significantly improve clinical outcomes in these patients because Nelotanserin actually suppresses instead of promoting the neuropsychiatric side effects of dopamine. It was clear from the presentation that Axovant Sciences has even a bigger outlook for Nelotanserin in the future. The possibility of having registrational trial data for Nelo (in its first of multiple applications) by the end of the year is truly exciting. Axovant Sciences is actively planning the design of phase 3 studies for Nelotanserin at this time.

Latest update: Nelotanserin granted Fast Track status by the FDA: BASEL, Switzerland, June 19, 2017 /PRNewswire/ -- Axovant Sciences (NYSE: [AXON](#)) today announced that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation to its investigational drug nelotanserin for the treatment of visual hallucinations disorder in dementia with Lewy bodies (DLB). (link: <http://www.prnewswire.com/news-releases/fda-grants-fast-track-designation-to-axovants-nelotanserin-for-visual-hallucinations-in-dementia-with-lewy-bodies-300475624.html>)

Belviq (lorcaserin)

Update: Lorcaserin as effective as phentermine or PT without the cardiovascular risks. Observational Comparative Effectiveness of Pharmaceutical Treatments for Obesity within the Veterans Health Administration <https://www.ncbi.nlm.nih.gov/pubmed/29044720>

Belviq – is an already approved (2012) best in class 5HT_{2C} agonist (partnered with Eisai). A once a day formulation was approved in mid-2016. Belviq is approved in the USA, Brazil, Mexico, South Korea, Israel, and pending in other locations throughout the World

Belviq sales have been hamstrung by slow market uptake, and minimal sales efforts by partner Eisai. To save cash Eisai cut its Belviq sales force from ~400 (in 2013) to 75 in 2016 (what the heck?). Excellent marketing and sales efforts by Eisai are apparently waiting on the outcome of required post-marketing long-term studies (6 years) on an FDA-mandated cardiovascular outcomes trial (CVOT) (Camelia is a 12,000 patient CVOT which is slated to complete in 2018). It is expected that a weight loss drug that has proven benefits in diabetes prevention and cardiovascular health has multi-blockbuster potential. Note the following:

- Belviq has patent protection through 2035, a once-a day formulation (Belviq XR) was approved in 2016 in the U.S.
- No more Belviq-associated study costs for ARNA. A deal was cut with Eisai earlier this year to alter the license agreement with Eisai and save ARNA potentially 80+ million dollars in potential downstream costs of development. Now:
 - ARNA can now focus all its efforts on its wholly owned pipeline going forward.
 - Tiered royalties on Belviq sales to ARNA are 9.5% to 18.5% depending upon sales (more sales = higher royalties). The royalty rates range from 9.5% on annual global net sales less than or equal to \$175 million, 13.5% on annual global net sales greater than \$175 million but less than or equal to \$500 million and 18.5% on annual global net sales greater than \$500 million.
 - Additional sales and regulatory milestones of between 20 and 30 millions of dollars are also available to ARNA under the Eisai agreement.
- Despite waiting on Camelia results, Eisai recently announced that it is expanding sales force in selected obesity markets in the U.S. as it awaits the results of the Camellia study in 2018.

Some physicians have been reluctant to prescribe Belviq because of lingering concerns about cardiac issues associated with older, less specific drugs like fenfluramine (which was taken off the market in 2012). On a bright note, Dr. Steven Vig (<https://belviqsuccess.wordpress.com/tag/dr-steven-vig/>) has prescribed Belviq over a thousand times and states that “Belviq is a very safe and effective drug”. What Dr. Vig is apparently well aware of and what has not been widely appreciated by the public and medical community yet is that lorcaserin (Belviq) was carefully designed/modeled to avoid the receptor (5HT2B) which is known to be responsible for heart related issues like valvulopathy that were associated with the use of fenfluramine.

Instead, Belviq’s activity was targeted very specifically against the 5HT2C receptor which is known to play a prominent role in overeating and drug addiction behavior. Even though preliminary Camelia data shows no adverse effects on heart function with the use of Belviq, Eisai, being a very conservative organization, prefers to wait for complete phase IV safety study results (2018) before aggressively promoting Belviq for weight loss, cardiac health and diabetes prevention. What is likely to come out of this phase IV analysis in 2018?

- No risk for valvular damage (available interim analyses already suggests this)
- Benefit in prevention of type II diabetes (available interim analyses, such as a reduction in the levels of glycosylated hemoglobin seen in patients taking Belviq, already suggests this)
- Benefit in prevention of heart attack
- Sales after heart studies (if positive) can easily surpass a billion dollars in sales a year. Over the longer term, sales are likely to be even higher because Eisai, along with various academic institutions and the National Institute of Drug Abuse (NIDA) are currently pursuing other high impact indications for Belviq such as smoking cessation and opioid and cocaine drug dependence.

Links describing clinical trials underway to study the use of lorcaserin (Belviq) in glycemic control in diabetes, opioid addiction, cocaine addiction, nicotine addiction (smoking), behavioral disorders (preclinical):

- <https://www.ncbi.nlm.nih.gov/pubmed/28345809>
- http://www.upi.com/Health_News/2017/03/24/Prescription-weight-loss-drug-may-help-with-opioid-addiction/6301490373701/
- <https://www.ncbi.nlm.nih.gov/pubmed/28371396>
- <https://www.ncbi.nlm.nih.gov/pubmed/28365033>
- <https://www.ncbi.nlm.nih.gov/pubmed/28294132>

Update on CVOT (June 2017) :

On June 22, 2017 Eisai issued a press release updating the progress of the Belviq Camellia CVOT trial (<http://www.eisai.com/news/news201729.html>). As we see it:

These "interim results" satisfy the initial FDA requirement for a CVOT trial in the first place and this PR confirms that Belviq does not increase the risk of Major Adverse Cardiovascular events by more than 1.4 times. This is a substantial improvement over the hazard ratio of close to 2.0 seen in the pivotal Contrave trial (NDA 200063). In its pivotal trial Qysmia (phentermine/topiramate) did not appear to increase the hazards ratio for MACE (not statistically significant) (Advisory Committee Meeting Feb 22, 2012) but this is surprising based upon the fact that phentermine was banned in Europe due to increased cardiovascular risk concerns. Topiramate (in the Qysmia phentermine/topiramate

compounded formula) is also a known mutagen. A follow-up CVOT trial was also mandated for Qysmia and is in progress.

It is not surprising that Eisai did not release an exact risk ratio in the interim results for Belviq as that release would compromise the ongoing study. If it was announced that Belviq actually reduced the risk of MACE (e.g 0.8) by 20%, many people in the study, who might have been on placebo, would want to drop out so they could start taking Belviq for certain. This would jeopardize the remainder of the study whose goal is to prove that Belviq does not increase the risk of MACE while lowering the risks of comorbidities associated with obesity. A premature release of interim data in the Contrave CVOT trial is what got OREX into so much trouble and ended up invalidating the entire trial. CVOT trial results for Contrave (mandated new trial) will not be available for approximately another 5 years. Without having the final word from the Camellia trial (in 2018), we have to assume at this time that Belviq will end up with a MACE ratio of somewhere in <1 to 1.4 range.

It is important to note that many weight loss drugs of the past have failed due to elevated MACE ratios (amphetamines, ephedrine, sibutaramine, etc). Considering that Contrave was approved in 2014 by meeting a MACE odds ratio of less than 2.0 I think that the "less than 1.4" category at least helps us be optimistic about the real goal of the Camellia trial (i.e. MACE+) as stated by Eisai: **If the primary safety objective is met, the efficacy objective is to evaluate the impact of lorcaserin on the incidence of MACE+, defined as MACE or hospitalization due to unstable angina or heart failure, or any coronary revascularization. In addition, other secondary objectives include the evaluation of lorcaserin on glycemic control in patients with type 2 diabetes mellitus and the potential to delay or prevent the conversion from pre-diabetes to type 2 diabetes.**

VALUATION

ARENA'S VALUE ON POSITIVE PHASE 2 and 3 DATA could be in the range of \$800 to over \$1000 PER SHARE. Positive Phase 2 data (3-5 trials report this year) should provide a meaningful boost to the current remarkably low share price. Recently, the chief medical officer of OREX (Preston Klassen, MD, MPH) joined the ARNA team as their CMO.

So what is ARNA worth now with the first phase 2 results only months away? Certainly not a measly \$15 a share. If we look at what other companies' similar and even inferior compounds are sold for, and compare them with those of ARNA's, the results border on the absurd, laughably so: Celgene snapped up Ozanimod (Etrasimod's competitor) two years ago for \$7.2 billion. For the sake of argument, call the two drugs equivalent and that puts ARNA at \$225 per share. Arena has approximately 32 million shares.

Ralinepag's competitor compound Selexipag (Uptravi) (now owned by Johnson and Johnson) has lesser targeting specificity and inferior PK parameters to Ralinepag. Selexipag was a key part of Johnson and Johnson's acquisition of Actelion in 2017 for \$30 billion. Let's be reasonable and say that at least \$8 billion of that price was due to the perceived value of Selexipag. Since Selexipag is an inferior compound to Ralinepag, let's be conservative and say that Arena's Ralinepag is worth perhaps \$8 billion as well. In Arena's terms that's \$250/share.

APD371, if it works as expected, could easily fetch a price of 5-10 billion dollars (\$156 - \$313/share).

If Belviq is shown to work in prevention of diabetes and heart attack (results known in 2018), then that part of the franchise could be worth at least \$3 billion on sale, even more if smoking cessation and drug abuse avenues are approved (\$94/share).

So, let's add this potential up: \$8 billion (Ralinepag) + \$7 billion (Etrasimod) + \$3 billion (Belviq) + \$7.5 billion (APD371) adds up to somewhere around \$25 billion dollars (\$781/share) if all upcoming phase 2 and phase 3 trial results are positive, as we hope. Discount the above about 40% (i.e. x .6) for risk of failure (since ARNA is running multiple phase 2 trials for Etrasimod) and another 25% for being later to the market place for Etrasimod and Ralinepag, so we estimate the current risk adjusted value for ARNA after phase 3 results at about \$25 billion x .6 (40% discounted) x .75 (25% discounted) or a bit over \$11 billion. So, let's be extra conservative and put the risk-adjusted value of ARNA at around \$5.5 billion (i.e. pre-phase 3 results).

The current market cap of ARNA is ~ \$0.49 billion adjusted for new shares recently added in April. The \$5.5 billion risk-adjusted value of ARNA (\$172/share) is around 11 times the current \$0.49 billion market cap (\$15/share). ARNA could be worth much more (an additional >5x) with positive phase 3 results down the road yielding a \$27.5 billion value (5x \$5.5 billion) which comes to \$860/share. Still, we don't expect ARNA to go it alone – any partnership deal for one of its compounds will bring certainty to the future and cash to push the remaining compounds through phase 3 results and approval. Oops, we forgot to add in another few billion dollars for our partnership with AXON if Nelotanserin continues to yield positive trial results.

Research has shown that positive phase 2 results often correlates with a significant increase in share price in emerging biotech companies (Couch et al. 2015). So, with 1 month before the first phase 2 readout in July 2017, and the rest of Arena's wholly owned programs announcing results before year-end 2017, it's obvious why we think Arena is a great buy at these very low prices.

Upcoming Timeline of Events

- Just initiated a Phase II study for APD371 in Crohn's Disease associated Pain (April-May 2017)
- Report Phase II Ralinepag Proof of Concept (POC) data in pulmonary arterial hypertension trial (mid 2017)
- Report Phase I PK/PD once daily Ralinepag formulation data in healthy volunteers (mid-2017)
- Axovant to report Phase II nelotanserin data in DLB and RBD (mid-2017)
- Initiate Phase II POC study for Etrasimod in primary biliary cirrhosis (PBC) (1H 2017)
- Report Phase II Etrasimod study results in ulcerative colitis (4Q, 2017)
- Report Phase II APD371 study results in Crohn's disease associated pain (4Q, 2017)
- Axovant to initiate Phase II trial of nelotanserin in DPB and RBD (4Q 2017)
- Report Phase II POC study of Etrasimod in dermatologic extra-intestinal manifestations of disease (EIMs)
- Report Phase II POC study results for Etrasimod in pyoderma gangrenosum (PG)
- Report Phase II POC study results for Etrasimod in PBC

ANALYST COVERAGE

Analysts coverage of ARNA has been the following (we don't maintain this section always up to date).

<u>Firm</u>	<u>Analyst</u>
Citigroup	Joel Beatty
JMP Securities	Jason Butler
JP Morgan	Jessica Fye
Cantor Fitzgerald	William Tanner
Leerink Partners	Joseph Schwartz
Needham & Company	Alan Carr
Piper Jaffray	Ted Tenthoff
WallachBeth Capital	Caroline Palomeque
Wells Fargo	Jim Birchenough

Leerink initiated coverage on ARNA on 19 May 2017 with a \$50 price target and Outperform rating. Mr. Joseph Schwartz is a star analyst. He was named #1 Stock Picker for Pharmaceuticals by FT/StarMine Analyst Awards. He was ranked as #1 analyst by Wall Street Journal for biotech stock picking.

Analyst Joseph Schwartz said following the strategic reorganization they see multiple opportunities for the company to generate significant shareholder value. Schwartz notes the company has greatly improved its exposure to its legacy Belviiq franchise by renegotiating its agreement with Eisai. It is also developing differentiated specialty medicines, which they could commercialize on its own or garner outside interest in. To wit: "Considering JNJ's [OP] recent acquisition of ATLN for ~\$30B, much of which was motivated by Uptravi (selexipag; for pulmonary arterial hypertension/PAH), we believe Phase 2 ralinepag data in 2Q17 has the potential to generate significant investor enthusiasm. Likewise, CELG's [MP] acquisition of RCPT for ~\$7B highlights the value that could be created by etrasimod (for moderate-to-severe ulcerative colitis/UC, among others) if Phase 2 data in multiple indications over the next 12-18 months are positive." Schwartz said a robust string of catalysts offers multiple opportunities for upside upon potential proof of concept.

Piper Jaffray analyst Ted Tenthoff called Arena Pharmaceuticals the "Turn Around Story of the Year: 3 Phase II Readouts in 2017". Mr. Tenthoff was ranked the No. 2 stock picker in biotechnology by the 2012 Wall Street Journal "Best on the Street" survey and was ranked the No. 1 stock picker for the life science tools and services sector in the 2006 StarMine Analyst Awards. FBR's Mr. Rahul Jasuja reiterated their outperform rating and \$60 price target in March 2017. Cantor Fitzgerald's Dr. Tanner initiated coverage with Overweight rating and \$37 price target. We believe these targets are conservative and will be raised if we get good data. Dr. Joel Beatty of Citigroup initiated coverage of ARNA in June 2017 with a Buy rating.

JMP Securities upgraded ARNA from Market Perform to Market Outperform (July 7, 2017) see link below).

*JMP analyst Dr. Jason Butler wrote: "We **believe ralinepag has the potential to be the best-in-class** oral prostacyclin agonist for the treatment of PAH, with a clinical profile most*

*similar to IV prostacyclin agonists. In our view, addressing selexipag's suboptimal efficacy, and being better positioned to demonstrate a mortality benefit in Phase 3 development, while still providing the convenience of an oral therapy, would support **a multi-billion dollar product opportunity.**"*

Butler also stated that *"Arena's current valuation misses the potential for clinical and commercial successes particularly with **"blockbuster asset" etrasimod.**"* Butler says that the company's focus on orphan indications can speed up development timelines and bring about a differentiated commercial opportunity compared to other S1P1 modulators. *"We believe the stock's current valuation under-appreciates the potential for clinical and commercial success of either of these assets,"* Butler added.

Keep in mind that we also have non-opioid APD371 for pain, and two big opportunities in Lewy body and Parkinson's disease-related dementia for our partner (with Axovant) Nelotanserin.

Our take is that all three wholly owned phase 2 assets are each potentially best in class and multi-billion-dollar opportunities in their own right. It is our opinion that ARNA is grossly undervalued at the current price and that the recent JMP and Cantor Fitzgerald analyst 12 month price targets (\$27 and \$37 respectively) are very conservative.

www.benzinga.com/analyst-ratings/analyst-color/17/07/9751450/arena-upgraded-analyst-sees-44-upside

INSTITUTIONAL OWNERSHIP (new update expected at any time)

A significant example of the progress Amit and Kevin are making attracting major institutional support was communicated to me in a meeting I had with Amit and Kevin at the Ladenburg Conference. Amit said that earlier this year they could not even get a meeting with the head of Fidelity's Biotech Fund. Just recently, that same person contacted Amit and invited him and Kevin to dinner.

The current top institutional owners of ARNA stock are (as of July 2017):

1. Great Point Partners, LLC
2. Wellington Management Group
3. Blackrock
4. Vanguard Group
5. Renaissance Technologies
6. State Street

The latest secondary offering (April 2017), was immediately fully allocated (including "greenshoe" allotment), is now in "strong hands" (according to the one of the bookrunners), i.e., institutions who are as optimistic as we are about prospects for strong data releases later this year. On April 18,

2017 Great Point Partners, LLC (www.gppfunds.com) filed form 13G disclosing their acquisition of 30,000,000 shares representing 9.75% of outstanding shares. They have indicated their optimism in Arena and admiring Amit Munshi's achievements to date.

INTELLECTUAL PROPERTY

Arena's patent portfolio has broad intellectual property coverage on composition and methods of use on all its chemical entities worldwide through 2029 at the earliest. Additional patent protection (e.g. on extended release formulations and new indications is ongoing).

INVESTOR RELATIONS

Under the previous management team, Arena's Investor Relations suffered from what appeared to be neglect, mismanagement (not surprising since the VP responsible for IR had no qualifications or experience in IR), and bad policies. The new team has recently brought in a top notch IR firm, i.e., LifeSci Advisors to oversee Arena's IR. We much welcome this new development, since we believe IR has been hurting for a long time. www.lifesciadvisors.com

INSIDER BUYS

CEO Amit Munshi recently made two open-market purchases of the stock (pre-RSS):

- 25,000 shares on 2017-05-12
- 50,000 shares on 2017-04-26

We view this as a bullish signal.

CONCLUSIONS

By our own estimates, we believe ARNA is a **STRONG BUY** with a potential nine month price target of \$100. This kind of price movement is not at all unusual in biotech. The key assumption is that the upcoming trial results are positive, that management executes to plan, continues to apply belt-tightening, brings on board a seasoned IR/marketing/promotion executive who can transform the demand channel (which was damaged by the previous management team), independent of data. The risks to our model are lack of good data from trials, and pitfalls from any residue of status quo inherited from past management team, including how relationships with investor community are handled, quality of communications, etc.

APPENDIX: Q2 2017 SUMMATION

ARNA now has close to \$300 million in cash and stated that it now has enough cash on hand to get through phase 3 trials for Ralinepag. ARNA management is approaching phase 3 trial design very carefully by first sifting through mountains of data available on treatments and progression of PAH from a worldwide perspective. ARNA management plans to discuss their upcoming, multi-tiered phase 3 designs with both European and U.S. regulatory agencies. It was exciting to hear that ARNA's main focus is to demonstrate superiority of Ralinepag to other currently available therapeutics for PAH. The phase 2 data that was presented by ARNA last July was only the tip of the iceberg and much more extensive data was collected during the course of the phase 2 trial. The first release of the more detailed Ralinepag data has already been submitted as a late-breaking abstract for an upcoming medical meeting (to be announced as soon as the abstract is accepted for presentation). With regard to readouts on phase 2 trials for Etrasimod and APD371...ARNA now states that this data may now be available in late 2017 instead of in Q1 of 2018 as earlier stated. Many good questions after the presentation by leading investment firms (JP Morgan, Jeffries, Needham). We encourage investors to listed to the call themselves on Arena's website under the Investors tab.

APPENDIX: FROM Q2 2017 PRESS RELEASE

Arena Pharmaceuticals Provides Corporate Update and Reports Second Quarter 2017 Financial Results

- **Achieved Positive Phase 2 Results for Ralinepag in July, Phase 3 Preparations Underway**
- **Clinical Results from Additional Phase 2 Programs Expected Over the Next Several Quarters**

SAN DIEGO , Aug. 7, 2017 /PRNewswire/ -- [Arena Pharmaceuticals, Inc.](#) (Nasdaq: ARNA), a biopharmaceutical company focused on developing novel, small molecule drugs across multiple therapeutic areas, today provided a corporate update and reported financial results for the second quarter ended June 30, 2017 .

"We are excited about the continued transformation of Arena in the past quarter, punctuated by the significant results achieved in the Phase 2 trial of ralinepag," said Amit Munshi , President and CEO of Arena. "With preparations underway for an end of Phase 2 meeting with the FDA for ralinepag, as well as multiple clinical data readouts from our other pipeline programs expected over the next several quarters, we are excited about the opportunity to continue driving shareholder value."

Pipeline Update

Ralinepag - oral, selective, next generation IP receptor agonist targeting the prostacyclin pathway for the potential treatment of pulmonary arterial hypertension

- In May, completed a pharmacokinetic and pharmacodynamic study comparing current twice-daily formulation with a new once-daily formulation in healthy volunteers
- In July, achieved positive Phase 2 results for ralinepag
- Currently preparing for end of Phase 2 meeting with the FDA ; Phase 3 clinical program preparations underway

Etrasimod - orally available next generation sphingosine-1-phosphate (S1P) receptor modulator for the potential treatment of a number of autoimmune diseases

- Phase 2 study in ulcerative colitis - data readout expected around year-end 2017 to Q1 2018
- Exploratory Phase 2 studies currently enrolling patients
 - Phase 2 study in dermatological extraintestinal manifestations in patients with inflammatory bowel disease
 - Phase 2 study in pyoderma gangrenosum
- Phase 2 study in primary biliary cholangitis
 - Expected to initiate in 2017

APD371 - orally available full agonist of the cannabinoid-2 receptor for the potential treatment of visceral pain, specifically pain associated with Crohn's disease

- Phase 2 trial currently enrolling patients - data readout expected around year-end 2017 to Q1 2018

APPENDIX: DRUG DEVELOPMENT PRIMER

Preclinical studies: performed in cell culture systems along with direct testing in living animals (typically rodents and other small mammals). Drug candidates are tested for animal safety and efficacy along with drug metabolism and distribution throughout the body. As a final step in preclinical testing, primates are often tested prior to moving the drug candidates into human testing. The drugs that make it through this testing cycle are patent protected as New Chemical Entities (NCEs) and they must be chemically unique from already existing NCEs. The best NCEs can move forward into human clinical studies (phase 1, phase 2, phase 3, phase 4) in a very orchestrated manner.

Phase 1 Human Clinical Trials: testing for drug distribution, metabolism and safety at a variety of doses in healthy volunteers. It makes sense to test healthy volunteers first since they don't bring a lot of other "noise" along (such as being on other drugs or having medical conditions that are not appropriate for the drugs being tested).

Phase 2 Human Clinical Trials: testing appropriate drug dose ranges identified in the Phase 1 trial for the proper balance of safety and efficacy in patients having the disease conditions relevant to the drug in question. These early studies contain enough patients to provide a good readout on efficacy and safety but typically not enough numbers to allow for filing a New Drug Application (NDA). In some cases (especially with Orphan Drugs), the phase 2 studies may be "powered" to a high enough level to allow filing of an NDA upon completion of these studies.

Phase 3 Human Clinical Trials: The trials that contain larger numbers of patients than earlier trials to allow strong statistically relevant information on safety and efficacy (typically versus a standard of care therapy for serious conditions) to be developed. Drugs that provide good evidence of efficacy with minimal safety issues in phase 3 trials are generally approved.

Phase 4 Human Clinical Trials: These trials (called post-marketing studies) are sometimes required after drug approval to address questions about the longer term consequences of the newly approved drug. In the case of weight loss drugs (e.g. Belviq and Contrave), the FDA is looking for long-term consequences of drug use in terms of safety and efficacy that may benefit by further study. In the case of Belviq, the **12,000 patient** phase 4 Camelia trial was designed to rule out any negative effects on heart function while providing enough data to establish if there are statistically significant improvements in heart function, prevention of heart attacks and decrease in transition to

type 2 diabetes. The Camelia trial began in 2014 and is expected to wrap up in 2018. A demonstrated benefit of Belviq in prevention of heart attacks and/or diabetes could easily elevate Belviq to blockbuster status.

Following are the Clinical Trial approximate approval rates during the various phases of drug development: Phase 1 to Phase 2 (63%), Phase 2 to Phase 3 (31%), Phase 3 to NDA accepted by the FDA (60%), NDA approval rate (85%). The overall approval rate is thus ~12% for non-oncology drugs. Phase 2 is obviously the point where most failures occur and thus it is easy to see why Phase 2 results are often the most critical for any drug development organization. Orphan drugs tend to have higher success rates at each stage of development.

(see for more detail:

<https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf>)