AEGIS CAPITAL CORP

Biopharmaceuticals
Nathan Weinstein, CFA
646-502-2522
nweinstein@aegiscap.com

Initiating Coverage

October 8, 2020

VistaGen Therapeutics, Inc.

Rating: Buy

Advancing Next Gen CNS Medicines

Key Metrics

VTGN - NASDAQ	$0.70
Pricing Date	Oct 7 2020
Price Target	$6.00
52-Week Range	$1.49 - $0.29
Shares Outstanding (mm)	74.0
Market Capitalization (mm)	$51.8
3-Mo Average Daily Volume	2,246,478
Book Value/Share	$0.30
Price/Book	2.3x

EPS FY: March

	2020A	Prior 2021E	Curr. 2021E	Prior 2022E	Curr. 2022E
1Q-Jun	(0.15)	--	(0.07)A	--	(0.05)E
2Q-Sep	(0.13)	--	(0.04)E	--	(0.05)E
3Q-Dec	(0.15)	--	(0.04)E	--	(0.05)E
4Q-Mar	(0.08)	--	(0.04)E	--	(0.06)E
FY	(0.50)	--	(0.19)E	--	(0.22)E
P/E	NM		NM		NM

Revenue (M)

	2020A	Prior 2021E	Curr. 2021E	Prior 2022E	Curr. 2022E
1Q-Jun	0.0	--	0.0A	--	0.0E
2Q-Sep	0.0	--	0.0E	--	0.0E
3Q-Dec	0.0	--	0.0E	--	0.0E
4Q-Mar	0.0	--	0.0E	--	0.0E
FY	0.0	--	0.0E	--	0.0E

Company Description:

VistaGen Therapeutics, Inc. (VTGN) is a clinical-stage biopharmaceutical company that is developing next generation therapies for central nervous system (CNS) conditions. The company's pipeline includes PH94B and PH10 neuroactive nasal sprays, and AV-101. Lead indications include Social Anxiety Disorder (SAD) and Major Depressive Disorder (MDD). VistaGen is headquartered in South San Francisco, CA and is traded on the Nasdaq exchange.

Investment Highlights:

- **VistaGen is developing multiple therapeutic candidates for the treatment of anxiety, depression, and other CNS indications.** VistaGen's development pipeline includes PH94B, a neuroactive nasal spray targeting Social Anxiety Disorder (SAD), among other conditions, PH10, an additional neuroactive nasal spray for indications including Major Depressive Disorder (MDD), and AV-101 an oral drug for psychiatric and other CNS disorders. We believe Phase 2 data in PH94B and PH10 strongly supports proof of concept, including compelling safety and efficacy data that likely differentiate these assets from existing treatments in crucial ways that could be supportive of market adoption if and when approved.
- **PH94B.** VistaGen's lead asset, PH94B, is a self-administered nasal spray designed to provide rapid-onset (<15 min), situational anxiety relief. PH94B leverages the nasal chemosensory system and has been shown to induce objective changes in key physiological metrics (e.g. decreased heart and respiratory rate, among others). In a Phase 2 study (n=91), patients on PH94B saw a significantly greater reduction in anxiety (on the SUDS scale) vs placebo (p=0.002). We think PH94B's usage profile (use as needed, right before SAD-triggering experiences), and safety/efficacy attributes, are currently underappreciated by the market. We next expect PH94B to move into a Phase 3 trial in 1H:21.
- **Social Anxiety Disorder (SAD).** Social anxiety disorder, or SAD, is an epidemic-level indication in the U.S. (impacting an est. 7.1% of adults in the last year). SAD is characterized by a phobia of being the center of attention, public speaking, being in a group setting, and so forth - out of proportion to the threat of these situations. We think PH94B stands out from the existing treatment landscape (that includes benzodiazepines, which may have dependency risk and other side effects), given: 1) its safety profile, 2) on-demand administration for acute situations, and 3) avoidance of systemic uptake. For these reasons, and others, our view is that PH94B could carve-out a strong niche in the SAD treatment landscape.
- **PH10.** In addition to PH94B, VistaGen is also advancing PH10 for numerous indications including Major Depressive Disorder (MDD). In a Phase 2A study, PH10 demonstrated an intriguing safety and efficacy profile, including statistically meaningful (p=0.022) improvement in patients (n=30) on the Hamilton Depression Rating Scale (HAM D). We next expect PH10 to move into a Phase 2B trial, in 2H:21.
- **Major Depressive Disorder (MDD).** MDD incidence in the U.S. is significant, with an est. 17.3mm adults having at least one major depressive episode. MDD carries a significant symptom burden, which may manifest both psychologically and physically. Remission rates with existing treatments have been estimated at 67%. We believe patients and practitioners are seeking alternative treatment options. We think PH10 could emerge as a differentiated option in MDD.
- **Valuation and target.** We initiate coverage on shares of VTGN with a BUY rating and $6.00 price target. Our valuation is based on a discounted cash flow model that explicitly credits PH94B in SAD and PH10 in MDD, while treating additional indications, and AV-101, as option value. Our model applies PoS estimates based on historical precedent data and uses a 25% discount rate. Risks include: 1) clinical, 2) financial, 3) regulatory, and 4) competition, among others.

The Disclosure section may be found on pages 25 - 26 of this report.

Summary

VistaGen Therapeutics (VTGN) is a clinical-stage biopharmaceutical company developing medicines focused on anxiety, depression, and other central nervous system ("CNS") disorders. VistaGen's clinical-stage candidates include PH94B, PH10, and AV-101. VistaGen Therapeutics is based in South San Francisco, CA, and trades on the Nasdaq exchange with the ticker symbol VTGN.

VistaGen is pursuing several psychiatric indications with its diverse, multi-faceted pipeline. For example, VistaGen's proprietary, differentiated neuroactive nasal spray (PH94B) is being developed for Social Anxiety Disorder, Adjustment Disorder with Anxiety, Generalized Anxiety Disorder, and other indications. VistaGen's PH10, an additional pipeline asset with a different API formulated as a neuroactive nasal spray, is being developed for Major Depressive Disorder, among other indications. Finally, VistaGen's AV-101, an oral drug, is being developed for multiple indications as well, including Major Depressive Disorder and other CNS indications.

Key investment points:

- VistaGen is developing medicines focused on psychiatric indications including anxiety and depression, as well as other CNS indications. In particular, VistaGen is focused on epidemic-level indications such as Social Anxiety Disorder (SAD) with an estimated 7.1% of US adults suffering from the condition in the last year, and Major Depressive Disorder (MDD), which impacts an estimated 17.3mm US adults, and which has high remission rates for existing standards of care.
- PH94B, which has Fast Track Designation, is currently the most advanced asset in VistaGen's portfolio, moving into Phase 3 trials, expected in 1H:21, for Social Anxiety Disorder. Phase 2 trials (n=91) for PH94B in SAD indicated a high degree of safety, with headache the only (mild) AE, and efficacy, including statistically meaningful (p=0.002) benefit vs placebo on the Subjective Units of Distress (SUDS) scale, which will also comprise the primary endpoint of the Phase 3 trials.
- PH94B, as well as PH10 – which are pherines (synthetic neuroactive steroids) – offer unique mechanisms of action via differentiated (intranasal) administration pathways, thereby engaging nasal chemosensory receptors, and have shown compelling Phase 2 data which underpin our confidence in an investment in VistaGen.
- PH10 is being developed for MDD, among other indications. We foresee PH10 moving into a Phase 2B trial in MDD in 2H:21. In a Phase 2A trial in patients (n=30) with MDD, PH10 led to a statistically meaningful (p=0.022 at the 6.5ug dose) reduction in the Hamilton Depression Rating Scale (HAM D).
- Additional value could accrue from successful data from Phase 2 trials of PH10 in Major Depressive Disorder, among other indications, additional Phase 2 trials of PH94B in indications beyond SAD, such as adjustment disorder with anxiety, and AV-101 in Major Depressive Disorder, among other indications, including in CNS indications, discussed further in this report.

Key risks:

As we see it, the risk profile of VistaGen is similar to other clinical-stage biotechnology companies, and includes:

(1) The potential for clinical trial failure and/or unfavorable data from PH94B, PH10, and/or AV-101 across one or multiple indications.

(2) Possibility for dilution that could result from accessing external sources of financing as is frequently the case amongst development-stage companies.

(3) Competition is also a risk, including from differing treatment modalities targeting the same indications.

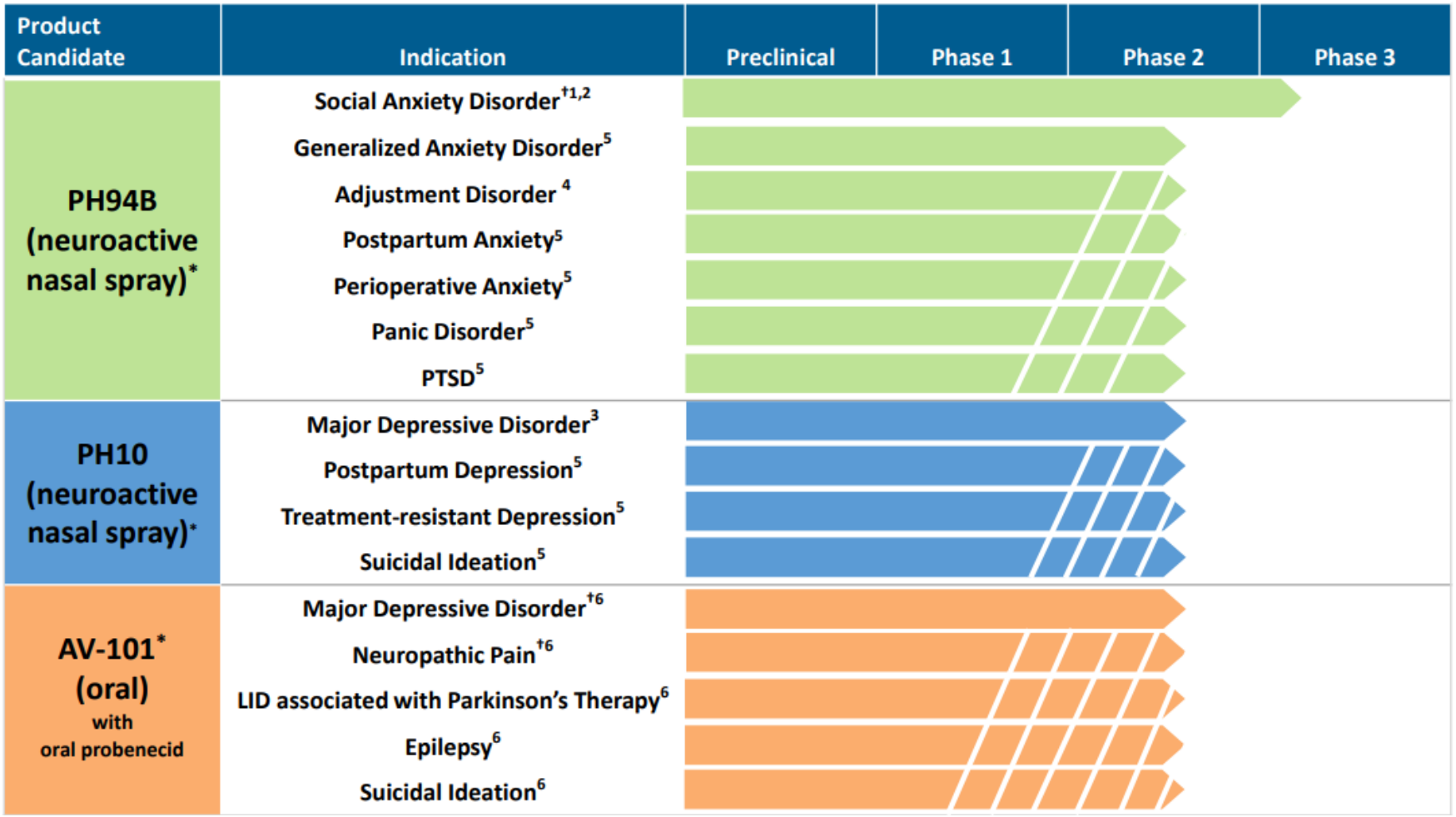
Background

VistaGen was founded by H. Ralph Snodgrass, Ph.D. in 1998, and underwent a change in focus (e.g. from stem cell-based treatments to anxiety, depression, and certain CNS disorders) in 2014. VistaGen's subsidiary, VistaStem, maintains a focus on pluripotent stem cell technology. The company is helmed by Shawn Singh, CEO and Director, with Dr. Snodgrass serving as President, CSO, and Director, and Mark Smith, M.D., Ph.D. serving as CMO. Jerrold Dotson serves as the company's CFO. VistaGen has assembled a clinical and regulatory advisory board and a scientific advisory board, discussed in depth later in this report.

Chairing the company's clinical and regulatory advisory board is Maurizio Fava, M.D., and the board is rounded-out by several highly accomplished members, including Michael Liebowitz, M.D.

VistaGen is developing multiple clinical assets, and undertaking pre-clinical work as well, across numerous psychiatric and CNS indications, discussed in-depth in this report.

Fig. 1. VistaGen pipeline



Source: VistaGen Therapeutics

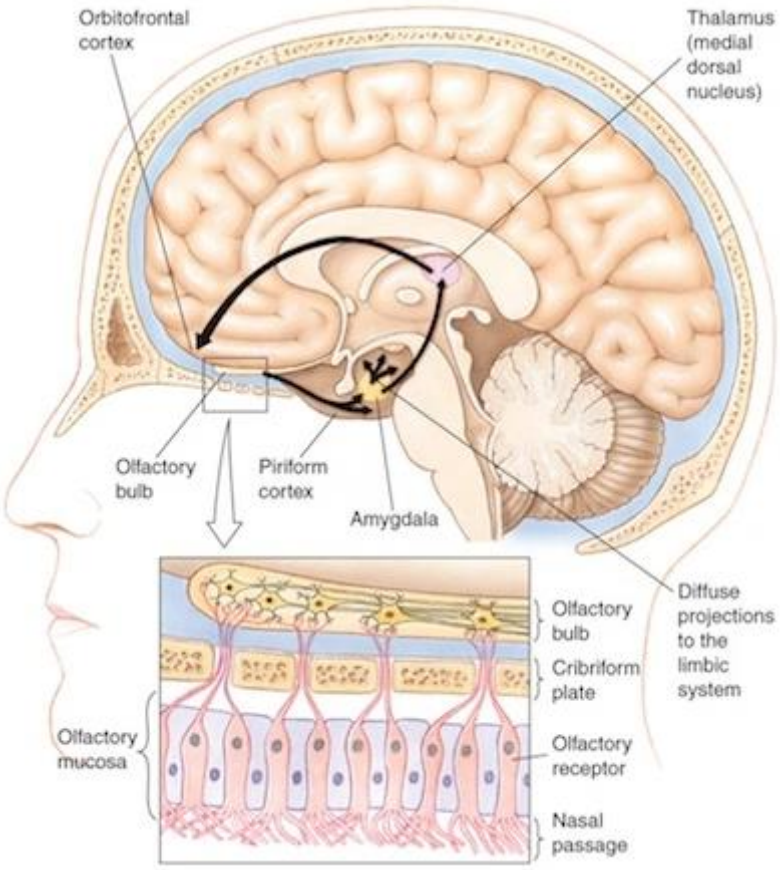
PH94B Neuroactive nasal spray

VistaGen's clinical-stage neuroactive nasal spray, PH94B, is designed to engage nasal chemosensory neurons with microgram doses of 3b-androsta-4,16-dien-3-ol. It is believed that in mammals, the hypothalamic-limbic areas of the brain receive direct afferent neural inputs from peripheral nasal chemosensory neurons, and that sensory transduction of external chemical cues in olfactory neurons triggers sensory inputs that reach the hypothalamus and the limbic amygdala through an oligosynaptic neural path. Administration of PH94B has been shown to induce heart rate decreases, and lower respiratory rate, electrodermal activity frequency, and eye blink frequency.[8]

Fig. 2. Example of PH94B administration

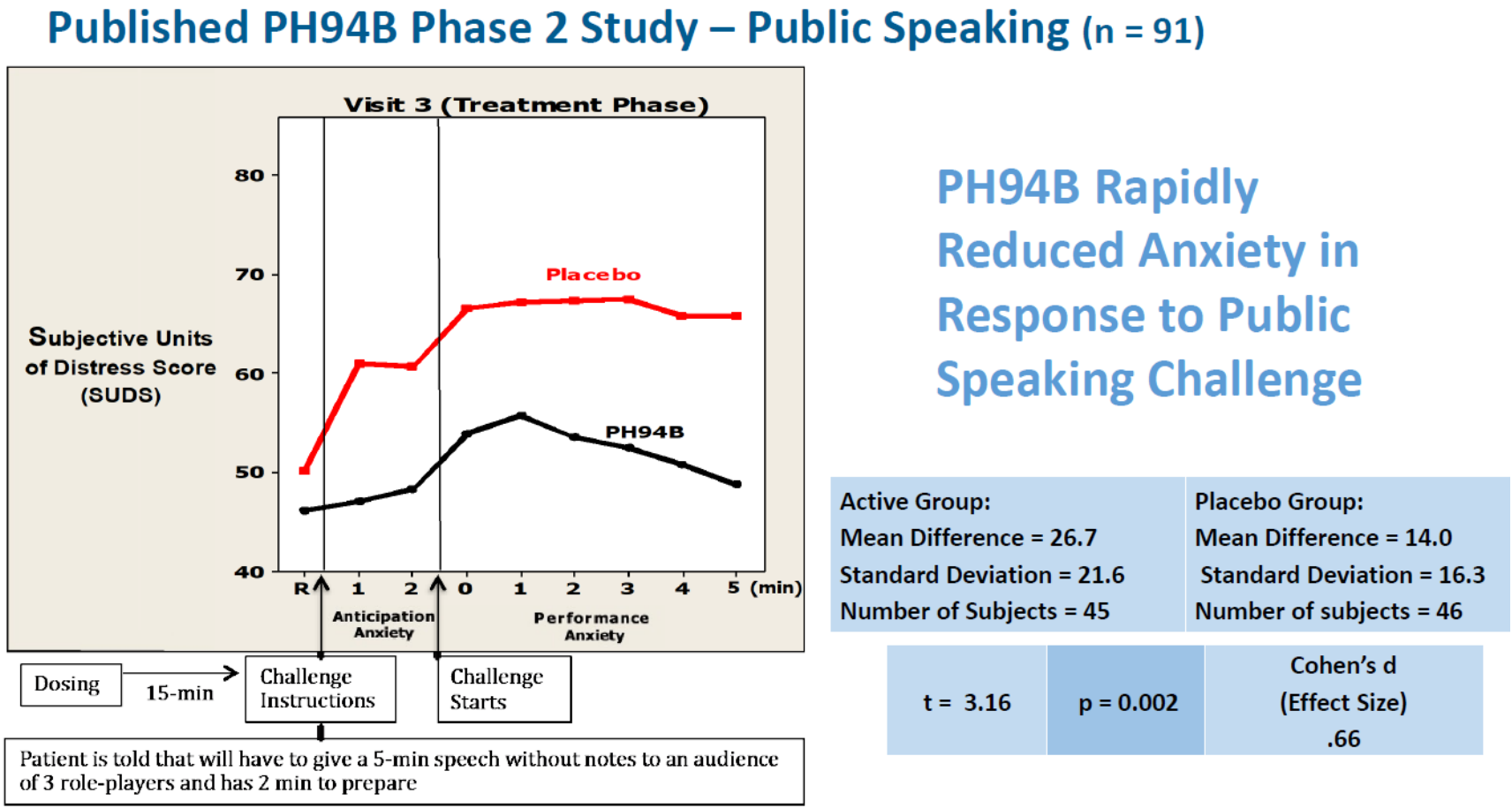
Source: Brain wiki

Fig. 3. Olfactory pathway



Source: VistaGen Therapeutics

Fig. 4. PH94B Phase 2 results



Source: VistaGen, American Journal of Psychiatry

In a Phase 2 (randomized, double-blind, placebo-controlled) trial, PH94B was more effective than placebo in reducing public-speaking (p=0.002) and social-interaction anxiety (p=0.009). This was assessed in patients with SAD, using Subjective Units of Distress (SUDS) scoring, with the challenges coming within 15-minutes of self-administration of 1.6 microgram doses of PH94B.

Fig. 5. PH94B Phase 3 study design

Principal Investigator: Dr. Michael Liebowitz, Columbia University, New York

- Recent FDA agreement will substantially reduce cost (50%), time and variability
- Design same as highly statistically significant (p=0.002) Phase 2 public speaking study
  - Assessing a single, identical, laboratory-simulated, anxiety-provoking public speaking challenge to all subjects
  - Single dose of PH94B (3.2 µg) or placebo administered after randomization
  - Primary efficacy endpoint assessed using Subjective Units of Distress Scale (SUDS)
- 12-15 sites in North America
- Target enrollment (completed subjects), 182

Source: VistaGen

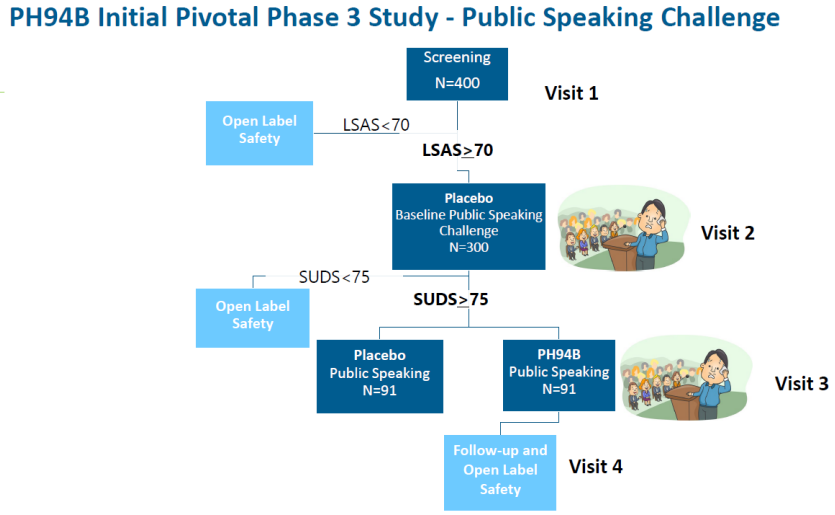
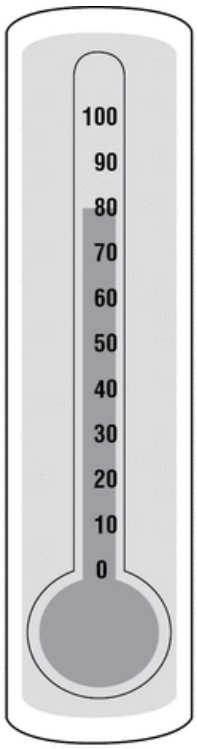


Fig. 6. Subjective Units of Distress (SUDS) scale



100 – Highest anxiety/distress that you have ever felt

90 – Extremely anxious/distressed

80 – Very anxious/distressed; can't concentrate. Physiological signs present.

70 – Quite anxious/distressed; interfering with functioning. Physiological signs may be present.

60 – Moderate-to-strong anxiety or distress

50 – Moderate anxiety/distress; uncomfortable, but can continue to function

40 – Mild-to-moderate anxiety or distress

30 – Mild anxiety/distress; no interference with functioning

20 – Minimal anxiety/distress

10 – Alert and awake; concentrating well

0 – No distress; totally relaxed

Note: "SUDS" stands for **"Subjective Units of Distress Scale."** Physiological signs may include, for example, sweating, shaking, increased heart rate or respiration, gastrointestinal distress.
Source: Oxford Clinical Psychology

PH94B: discussion

As will be covered later in the 'Indications' section of this initiation report, Social Anxiety Disorder (SAD) is a major – pandemic level – health issue, involving 7.1% of US adults in the past year, and 12.1% of US adults in their lives, according to the National Institute of Mental Health. Many types of anxiety have early onset, for example 13 years old in SAD.[9]

The treatment landscape for anxiety is likewise discussed in the 'Indications' section, however, our general view is that there are several treatment options, which include psychotherapeutic and pharmacologic treatments, and combinations thereof.

In SAD, patients are afraid of situations in which they are the center of attention. There are a variety of feelings attached to that, according to researchers, such as fear of appearing clumsy, drawing criticism, embarrassing themselves, or being judged in a negative fashion.[9]

Pharmacological treatments used in anxiety in adults may include: SSRIs, SNRIs, anti-depressants, calcium modulator, azapirone, and RIMA. The adverse effects (AEs) of these drug classes is well documented, and may include jitteriness, nausea, restlessness, headache, fatigue, weight changes, tremor, sweating, sexual dysfunction and others.[9]

In particular, benzodiazepines are used in an estimated 55% to 94% of patients with anxiety disorders in the U.S. Side effects of "benzos" (e.g. Xanax, Valium, Klonopin, etc.) include fatigue, dizziness, increased reaction time, and cognitive impairment mainly in older patients. Additionally, use beyond 4-8 months may lead to dependency.[9]

In "Effect of an Acute Intranasal Aerosol Dose of PH94B on Social and Performance Anxiety in Women With Social Anxiety Disorder" (Michael Liebowitz, M.D., et al) showed a greater decrease in mean Subjective Units of Distress (SUDS) in patients treated with PH94B than patients on placebo. In addition, importantly, PH94B's side effects were found to be benign and the intranasal spray was administered just 15 minutes before laboratory stimulated public speaking and social interaction challenges.

Taking all of this data, and reviewing the existing landscape, we believe PH94B is a highly differentiated asset which: (1) works very quickly (e.g. within 15 minutes of administration), (2) does not bear the same side effect profile seen with the benzos, and (3) will find itself, if approved, being commercialized in a backdrop characterized by no other approved treatment with quite the same safe and acute-use characteristics. Therefore, it's not hard for us to imagine the light, small nasal applicator traveling around with SAD patients on their person, throughout their day, and being used on an as-needed basis. The fact that SUDS is the endpoint in the Phase 3, and that existing Phase 2 proof of concept data around SUDS was so positive, further reinforces our bull case.

PH94B was licensed to EverInsight/CBC Group in June 2020 in Asian markets. There was a $5mm up-front payment, and potential milestones of $172mm and royalties on commercial sales. EverInsight will take responsibility for the Phase 3 and regulatory submission activities in Greater China, South Korea, and Southeast Asia.[2]

PH10 neuroactive nasal spray

PH10 is a synthetic neurosteroid (Pregn-4-en-20-yne-3-one), delivered intranasally, that is being developed for a wide variety of depression-related indications. The initial indication for PH10 is major depressive disorder (MDD), although other depression disorders such as postpartum depression (PPD), suicidal ideation (SI), and others, could follow. We believe VistaGen will next seek to advance PH10 through Phase 2B for the treatment of MDD in the US, and anticipate commencement of this trial in late 2021.

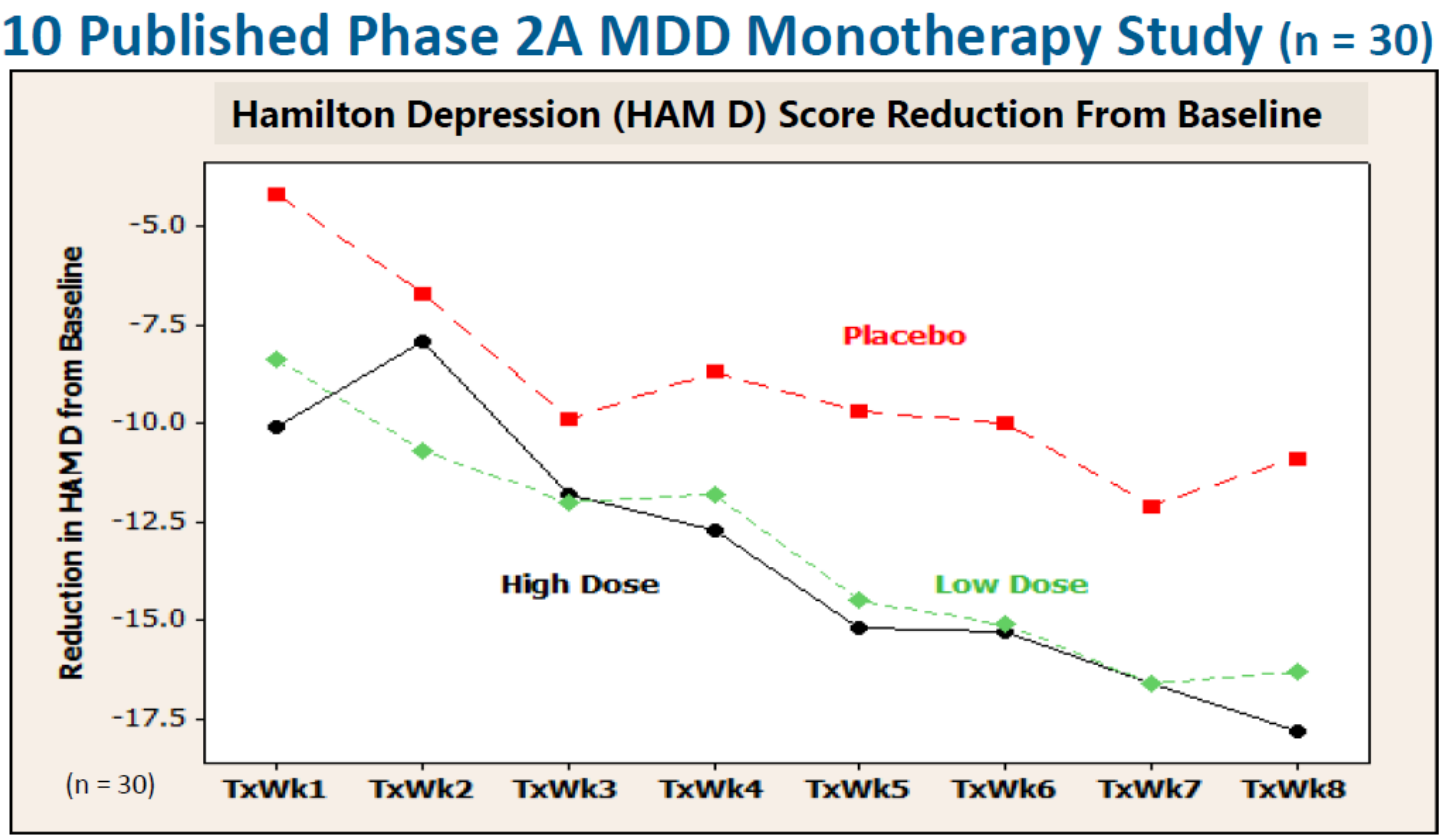
The World Health Organization (WHO) counts 300mm people as suffering from depression, and in the U.S. The National Institute of Mental Health estimated that 17.2mm adults had at least one major depressive episode in 2017. MDD differs from a depressed mood in that it consists of chronic, pervasive feelings of unhappiness and suffering, leading to impaired functioning.

Developed from pherine compounds, PH10 is an odorless, neuroactive nasal spray that actives chemosensory receptors that trigger neural pathways in the brain, and is thought to produce antidepressant effects. The pathway consists of microgram doses of API engaging nasal chemosensory neurons (NCNs) which activate olfactory bulb neurons (OBNs) on the base of the brain, which in turn connect through neurons to the central limbic amygdala (where mood is regulated).[2]

In a Phase 2A study, PHD10 (self-administered at 6.4 micrograms of dose) was considered safe and led to rapid onset of antidepressant effects, sustained over an 8-week period, as measured by the Hamilton Depression Rating Scale-17 (HAM-D-17) with a p-value of 0.022 (statistically meaningful).[2]

Importantly, when considering how PH10 could fit into the treatment paradigm, we reference the rapidity of action and safety profile shown from the Phase 2A trial. In particular, we think the ability to have a rapid-onset antidepressant, including one free from the side effect profile inherent in ketamine-based treatments, could see meaningful use, in our view. This becomes especially true in light of the high remission rates (67%) patients experience on the existing commercial-stage therapies.

Fig. 7. PH10 Phase 2A results



PH10 Dose	HAM D Score	P (PH10 vs Placebo)	Cohen's D (Effect Size)
3.2 µg (Low Dose)	16.3	.101	0.74
6.4 µg (High Dose)	17.8	.022	0.95
Placebo	10.9		

Source: VistaGen, Phar Med Res

AV-101

AV-101 (4-Cl-KYN) is an oral prodrug targeting NMDAR, an ionotropic glutamate receptor in the brain. Unlike ketamine and other antagonists, AV-101 doesn't block NMDAR. AV-101 has received Fast Track designation as a potential adjunctive treatment for MDD and an opioid-alternative for neuropathic pain. VistaGen has outlined a strategy to advance AV-101, in combination with probenecid (an oral uric acid lowering agent, which is known to block activity of certain organic ion efflux transporters in the kidney), through Phase 2 B clinical development in one or more CNS indications where abnormal NMDAR is implicated.[2]

In a study from 2019, AV-101 failed to differentiate from placebo in a Phase 2 clinical trial, along with a standard oral antidepressant, in MDD. This was the Elevate study. Following further analysis, VistaGen concluded that the trial failure may have been due to sub-therapeutic concentrations of API in the brain.[2]

Additional research conducted both by Baylor College of Medicine, and VistaGen's own pre-clinical work suggests that combining AV-101 with adjunctive probenecid could increase the therapeutic concentrations and duration in the brain. For example, it was found in the Baylor phase 1B, that in health volunteers, higher doses of AV-101 could increase 40 Hz auditory steady state response, a measure of the integrity of inhibitory interneuron synchronization associate with NMDAR inhibition.

We believe VistaGen will continue to study AV-101, including undertaking preclinical studies in various NMDAR-focused CNS indications (see pipeline).

Indications

As shown in the 'Pipeline' section of this report, PH94B is being studied in numerous indications, including Social Anxiety Disorder, Adjustment Disorder with Anxiety, Generalized Anxiety Disorder, Adjustment Disorder, Postpartum Anxiety, Perioperative Anxiety, Panic Disorder, Post Traumatic Stress Disorder, Major Depressive Disorder, Postpartum Depression, Treatment-resistant Depression, Suicidal Ideation, Neuropathic Pain, LID associated with Parkinson's Therapy, and Epilepsy.

Below, we discuss the lead indications for PH94B, PH10, and AV-101 (oral).

Social Anxiety Disorder ("SAD")

According to The Anxiety and Depression Association of America, approximately 15 million American adults suffer from SAD, and onset is typically during the teenage years.[3] Meanwhile, the National Institute of Mental Health ("NIMH") pegs SAD incidence at 7% of Americans, or 22.4mm people (based on a 320mm population estimate).[5]

Physical symptoms associated with SAD include rapid heartbeat, muscle tension, lightheadedness, among others.[4]

Mental and emotional symptoms associated with SAD include fear [of social situations], dizziness/sickness, difficulty meeting with and/or talking to people, and self-medicating behavior (e.g. drinking).[5]

Besides social situations, symptoms could also, or in place of, present in performance situations – e.g. giving a speech, playing sports, or performing on stage.[5]

Additional potential "triggers" could include: starting or maintain a conversation, participating in small groups, eating in front of others, giving a presentation, asking someone out, being the center of attention, urinating in the presence of others, and any situation with potential for appearing nervous to others or being observed blushing, sweating, or shaking.[6]

Major Depressive Disorder ("MDD")

Depression, or Major Depressive Disorder, or MDD, is a mood disorder characterized by feelings of sadness, and loss of interest. According to The Mayo Clinic, depression is not simply a "case of the blues" from which patients can simply "snap out," but, rather, a condition that may require long-term treatment. Treatment may include medication (see more in the section on competition) and psychotherapy, among other types of treatment.[7]

Symptoms of MDD are known to include: sadness, tearfulness, emptiness, hopelessness, angry outbursts, irritability, frustration, lack of interest or pleasure, sleep disturbances, or sleeping too much, tiredness, lack of energy, changes in appetite, weight, food cravings, anxiety, agitation, restlessness, slowed thinking, speaking, or body movements, and others. Other symptoms can include trouble thinking, concentrating, feelings of worthlessness or guilt, fixating on past failures, self-blame, and physical problems such as back pain or headaches.[7]

Incidence of MDD in the U.S. is significant. According to the National Institute of Mental Health, an estimated 17.3mm adults in the U.S. had at least one major depressive episode in the past year. MDD disproportionately impacts females (8.7%) than males (5.3%).[10]

CNS indications

Here, we point out briefly some of the CNS indications that could become a target for development now and in the future, given VistaGen's current portfolio, and these include neuropathic pain, Levodopa-induced Dyskinesia (LID) associated with Parkinson's Therapy, Epilepsy, and Suicidal ideation.[2]

Market and competition

Existing SAD treatment options include non-medication methods such as psychotherapy and support groups, as well as medication including anti-anxiety medications, antidepressants, and beta-blockers.[5] VistaGen has stated that the commercial opportunity for PH94B in the US SAD market is $2.17bn-$3.1bn, citing a commercial assessment from i3 Strategy (Winter 2019). The revenues produced by prescription drugs that serve the SAD, or relate end-markets, are significant. For example, Zoloft, a selective serotonin reuptake inhibitor (SSRI), with a broad label covering MDD, SAD, PTSD, and other conditions saw sales of $3.3bn in 2005. Additionally, Lexapro, an SSRI with a label including MDD, and GAD, saw $3bn of sales in 2011. There are many generics in the broader psychiatry space, including many antidepressants.

The existing medication options have pros and cons. For example, the anti-anxiety medications may work quickly, but patients could develop tolerance. The antidepressants may take a long time to work (several weeks or longer), and could have side effects including headaches and nausea. Beta blockers (beta-adrenergic blocking agents) are known to reduce heart rate, open up veins and arteries, and improve bloodflow.[5] These agents block the effects of the hormone epinephrine (adrenaline); brand name example including Sectral, Tenormin, Bystolic, and others. With use in several indications, including outside psychiatry, the relevant indication/use-case here, is in anxiety.

According to Anxiety and Depression Association of America's (ADAA) clinical practice review for Social Anxiety Disorder, first line treatment includes psychotherapy, such as cognitive behavioral therapy (CBT). On average, CBT consists of 15-20 sessions. Aspects of CBT includes psychoeducation about the condition, as well as exposure to feared situations. There are both individual and group CBT settings.[6]

Additionally, front-line treatments include pharmacotherapy. Therapies utilized as front-line treatments for SAD include SSRIs and SNRIs. Drugs in this class, approved by the FDA for SAD and other conditions include sertraline (Zoloft), fluvoxamine controlled release, and venlafaxine extended release. Other medications in these classes with evidence of efficacy from randomized controlled trials include citalopram (Celexa), escitalopram (Lexapro), and vilazodone (Viibryd). Fluoxetine (Prozac) has had mixed results in randomized controlled trials.[6]

Second-line treatments include variations of CBT. Options may include group therapy, or therapy delivered over the internet. Additionally, mindfulness and acceptance-based therapies may be employed. Further options delineated as psychotherapy delineated as second-line include applied relaxation training, social skills training, interpersonal psychotherapy, psychodynamic psychotherapy. In terms of second-line pharmacotherapy options, another SSRI or SNRI could be employed (e.g. if the patient did not respond to the first-line option).[6]

Second-line pharmacotherapy options may also include other antidepressants such as Mirtazapine (e.g. Remeron), Moclobemide (e.g. Amira), Phenelzine (e.g. Nardil). Another option are the Benzodiazepines, such as Clonazepam (Klonopin), alprazolam (Xanax), and bromazepam, although risks of abuse and lack of efficacy for comorbid depression are cited.[6]

Gabapentin (e.g. Gralise) and pregabalin (Lyrica) have been cited as efficacious. Olanzapine (Zyprexa) and quetiapine (Seroquel) are also included as options. Additionally, the beta adrenergic blockers such as propranolol (Inderal) and atenolol (Tenormin) are mentioned as efficacious, in some situations. Finally, agents including bupropion SR (e.g. Wellbutrin), clomipramine (Anafranil), topiramate (e.g. Trokendi), and divalproex were cited as second-line options with limited evidence for efficacy.[6]

Only three drugs, all oral antidepressant drugs (ADs), are approved by the U.S Food and Drug Administration (FDA) specifically for treatment of SAD, and no drug is FDA-approved for acute, on-demand treatment of SAD, we believe.

There are three antidepressants specifically approved by the FDA for SAD, although none approved for acute, on-demand treatment. We note the generally slow onset of these drugs. While benzos and beta-blockers are often prescribed off-label, they may – benzos in particular – have safety issues regarding dependence, and alcohol-like side effects.

In a drug safety communication issued by the FDA on September 23rd, 2020, the agency announced that the FDA would be requiring a boxed warning update to improve the safe use of the benzodiazepine (benzo) drug class, including noting the potential for abuse, addiction, and other serious risks.

The key differentiator, in our view, for PH94B is how fast it works, and that, to the extent we have seen, it does not carry dependency risks, and that its side effect profile is much cleaner than alternatives, meaning it works fast and doesn't incapacitate the user, making it ideal for administration shortly before anxiety-inducing activities, which could include everything from speaking to one or a few people, to large public gatherings, and everything in-between.[2]

Likewise, for PH10, we believe the drug's differentiated profile, as demonstrated in the successful Phase 2A trial, will lend itself to use – if and when approved. We note that studies have shown that 67% of patients fail their first antidepressant. We think PH10 could see use as a first alternative following an initial failure to an existing commercial antidepressant. The safety profile in particular in compelling, and we think (1) safety/low side effects, (2) efficacy, and (3) rapidity of efficacy, are important considerations in the antidepressant landscape.

Management

Shawn K. Singh is Chief Executive Officer and Director at VistaGen Therapeutics, Inc. and Chief Operating Officer & General Counsel at Cato Holding Co. Mr. Singh is also on the board of Armour Therapeutics, Inc. and Member of The State Bar of California. Previously, he was Chief Executive Officer at VistaGen, Inc., Director at Echo Therapeutics, Inc. Chairman of Sontra Medical Corp. Chairman of Durham Pharmaceuticals and Chairman of Echo Therapeutics, Inc. (all subsidiaries of Echo Therapeutics, Inc.), Corporate Finance Associate at Morrison & Foerster LLP, Chief Business Officer for SciClone Pharmaceuticals, Inc., Managing Director at Start-up Law, Principal at Celerity Fund, Inc., Chief Business Officer & General Counsel at Cato Research LLC and Managing Principal at Cato BioVentures (a subsidiary of Cato Research LLC), Chief Executive Officer & Director at Excaliber Enterprises Ltd., Chief Executive Officer of VistaGen Therapeutics, Inc. and President at Artemis Neuroscience, Inc. Mr. Singh received an undergraduate degree from the University of California, Berkeley and a graduate degree from The University of Maryland Francis King Carey School of Law.

H. Ralph Snodgrass is Founder, President, Director & Chief Scientific Officer at VistaGen Therapeutics. Dr. Snodgrass was previously Chief Executive Officer for VistaGen, Inc., Executive Director & Chief Scientific Officer at Progenitor, Inc., Professor at Lineberger Comprehensive Cancer Center, President, Director & Chief Scientific Officer at Excaliber Enterprises Ltd., President & Chief Scientific Officer at VistaGen Therapeutics, Inc., Member of Basel Institute for Immunology and Professor at UNC School of Medicine. Dr. Snodgrass received a doctorate from the University of Pennsylvania.

Jerrold D. Dotson is Chief Financial Officer, Secretary & VP at VistaGen Therapeutics, Inc. Previously, Mr. Dotson was Secretary, Vice President-Finance & Administration at Calypte Biomedical Corp., Chief Financial Officer of California & Hawaiian Sugar Co. and Controller at Discovery Foods LLC. Mr. Dotson received an undergraduate degree from Abilene Christian University.

Mark A. Smith is Chief Medical Officer of VistaGen Therapeutics, Inc. In the past, Dr. Smith held the position of Executive Director-Clinical Development at AstraZeneca Plc and Senior Director-Experimental Medicine at Shire Plc. He received an undergraduate degree and a graduate degree from Yale University and a doctorate from the University of California San Diego.

Mark A. McPartland is Vice President-Corporate Development for VistaGen Therapeutics, Inc. He was previously Vice President & Partner at Alliance Advisors LLC, Regional Vice President at Hayden Communications, Inc., Senior Vice President-Southeast US at MZ Group and VP-Corporate Development & Communications at Stellar Biotechnologies, Inc. Mark A. McPartland received an undergraduate degree from Coastal Carolina University.

Modeling assumptions

We credit PH94B and PH10 in our valuation, while treating AV-101 as option value, at this stage. We use historical precedents regarding est. WAC. We assume patent expiry for PH94B in a 2028 timeframe, and for PH10 in a 2033 timeframe. Our choice of discount rate (25%) and market share are meant to reflect a conservative stance. PoS estimates are derived from industry data (BIO).

Fig. 8. Revenue model

	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033
PH94B (U.S. market - Social Anxiety Disorder)														
SAD patients	15,678,000	15,991,560	16,311,391	16,637,619	16,970,371	17,309,779	17,655,974	18,009,094	18,369,276	18,736,661	19,111,395	19,493,622	19,883,495	20,281,165
Market share					*1%*	*2%*	*3%*	*4%*	*5%*	*4%*	*3%*	*2%*	*1%*	*1%*
PH94B patients					169,704	346,196	529,679	720,364	918,464	796,308	649,787	477,594	288,311	294,077
Avg. months of treatment					2	6	6	6	6	6	6	6	6	6
WAC /mo					$380	$380	$380	$380	$380	$135	$135	$135	$135	$135
PoS					*49.0%*	*49.0%*	*49.0%*	*49.0%*	*49.0%*	*49.0%*	*49.0%*	*49.0%*	*49.0%*	*49.0%*
Revenue					**$63,197,663**	**$386,769,698**	**$591,757,638**	**$804,790,388**	**$1,026,107,745**	**$316,054,687**	**$257,900,624**	**$189,556,959**	**$114,430,507**	**$116,719,117**
Growth						*512%*	*53%*	*36%*	*28%*	*-69%*	*-18%*	*-27%*	*-40%*	*2%*

	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033
PH10 (U.S. market - Major Depressive Disorder)														
MDD patients (2L)	11,524,000	11,754,480	11,989,570	12,229,361	12,473,948	12,723,427	12,977,896	13,237,454	13,502,203	13,772,247	14,047,692	14,328,646	14,615,218	14,907,523
Market share						*1%*	*2%*	*3%*	*4%*	*5%*	*6%*	*7%*	*8%*	*9%*
PH10 patients						127,234	259,558	397,124	540,088	688,612	877,981	1,060,320	1,227,678	1,401,307
Avg. months of treatment						2	4	4	4	4	4	4	4	4
WAC /mo						$380	$380	$380	$380	$380	$380	$380	$380	$380
PoS						*11.6%*	*11.6%*	*11.6%*	*11.6%*	*11.6%*	*11.6%*	*11.6%*	*11.6%*	*11.6%*
Revenue						**$11,216,973**	**$45,765,251**	**$70,020,835**	**$95,228,335**	**$121,416,127**	**$154,805,562**	**$186,955,582**	**$216,464,246**	**$247,078,476**
Growth							*308%*	*53%*	*36%*	*28%*	*28%*	*21%*	*16%*	*14%*

Source: Aegis Capital estimates

Fig. 9. Clinical development success rates (2006-2015)

Phase Success	Phase I to Phase II		Phase II to Phase III		Phase III to NDA/BLA		NDA/BLA to Approval	
	Advanced or Suspended	Phase Success	Advanced or Suspended	Phase Success	Advanced or Suspended	Phase Success	Advanced or Suspended	Phase Success
Hematology	86	73.3%	83	56.6%	64	75.0%	50	84.0%
Infectious disease	347	69.5%	286	42.7%	150	72.7%	133	88.7%
Ophthalmology	66	84.8%	101	44.6%	60	58.3%	40	77.5%
Other	96	66.7%	116	39.7%	46	69.6%	43	88.4%
Metabolic	95	61.1%	84	45.2%	35	71.4%	27	77.8%
Gastroenterology*	41	75.6%	56	35.7%	33	60.6%	26	92.3%
Allergy	37	67.6%	40	32.5%	14	71.4%	16	93.8%
Endocrine	299	58.9%	242	40.1%	143	65.0%	107	86.0%
Respiratory	150	65.3%	196	29.1%	45	71.1%	37	94.6%
Urology	21	57.1%	52	32.7%	21	71.4%	14	85.7%
Autoimmune	297	65.7%	319	31.7%	135	62.2%	86	86.0%
All Indications	**3582**	**63.2%**	**3862**	**30.7%**	**1491**	**58.1%**	**1050**	**85.3%**
Neurology	462	59.1%	465	29.7%	216	57.4%	161	83.2%
Cardiovascular	209	58.9%	237	24.1%	110	55.5%	76	84.2%
Psychiatry	154	53.9%	169	23.7%	70	55.7%	58	87.9%
Oncology	1222	62.8%	1416	24.6%	349	40.1%	176	82.4%

Likelihood of Approval	Phase I to Approval		Phase II to Approval		Phase III to Approval		NDA/BLA to Approval	
	LOA n	Phase LOA	LOA n	Phase LOA	LOA n	Phase LOA	LOA n	Phase LOA
Hematology	283	26.1%	197	35.7%	114	63.0%	50	84.0%
Infectious disease	916	19.1%	569	27.5%	283	64.5%	133	88.7%
Ophthalmology	267	17.1%	201	20.1%	100	45.2%	40	77.5%
Other	301	16.3%	205	24.4%	89	61.5%	43	88.4%
Metabolic	241	15.3%	146	25.1%	62	55.6%	27	77.8%
Gastroenterology*	156	15.1%	115	20.0%	59	55.9%	26	92.3%
Allergy	107	14.7%	70	21.8%	30	67.0%	16	93.8%
Endocrine	791	13.2%	492	22.4%	250	55.9%	107	86.0%
Respiratory	428	12.8%	278	19.6%	82	67.3%	37	94.6%
Urology	108	11.4%	87	20.0%	35	61.2%	14	85.7%
Autoimmune	837	11.1%	540	17.0%	221	53.5%	86	86.0%
All Indications	**9985**	**9.6%**	**6403**	**15.3%**	**2541**	**49.6%**	**1050**	**85.3%**
Neurology	1304	8.4%	842	14.2%	377	47.8%	161	83.2%
Cardiovascular	632	6.6%	423	11.2%	186	46.7%	76	84.2%
Psychiatry	451	6.2%	297	11.6%	128	49.0%	58	87.9%
Oncology	3163	5.1%	1941	8.1%	525	33.0%	176	82.4%

Source: Bio

PH10(P2) **PH94B (P3)**

Fig. 10. Valuation

FY	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033
Revenue				**$63,197,663**	**$397,986,672**	**$637,522,890**	**$874,811,223**	**$1,121,336,080**	**$437,470,814**	**$412,706,187**	**$376,512,541**	**$330,894,754**	**$363,797,593**
Growth					*530%*	*60%*	*37%*	*28%*	*-61%*	*-6%*	*-9%*	*-12%*	*10%*
COGS				$9,479,649.47	$47,758,400.60	$63,752,288.98	$43,740,561.14	$56,066,804.00	$21,873,540.71	$20,635,309.35	$18,825,627.03	$16,544,737.68	$18,189,879.64
Gross profit				$53,718,013.64	$350,228,271.04	$573,770,600.79	$831,070,661.69	$1,065,269,276.06	$415,597,273.55	$392,070,877.59	$357,686,913.64	$314,350,015.88	$345,607,713.21
Gross margin				*85%*	*88%*	*90%*	*95%*	*95%*	*95%*	*95%*	*95%*	*95%*	*95%*
SG&A	5,819,425	6,549,814	6,877,305	7,565,035	7,943,287	8,340,452	8,757,474	9,195,348	9,655,115	10,137,871	10,644,765	11,177,003	11,735,853
R&D	8,033,571	14,380,677	14,812,097	15,256,460	14,493,637	13,768,955	13,080,507	12,426,482	11,805,158	11,214,900	10,654,155	10,121,447	9,615,375
Total operating expenses	13,852,996	20,930,491	21,689,402	22,821,495	22,436,924	22,109,407	21,837,981	21,621,830	21,460,273	21,352,771	21,298,920	21,298,450	21,351,228
EBIT	(13,852,996)	(20,930,491)	(21,689,402)	30,896,518	327,791,347	551,661,194	809,232,680	1,043,647,446	394,137,000	370,718,107	336,387,994	293,051,566	324,256,485
Operating margin				*49%*	*82%*	*87%*	*93%*	*93%*	*90%*	*90%*	*89%*	*89%*	*89%*
Interest													
EBT	(13,852,996)	(20,930,491)	(21,689,402)	30,896,518	327,791,347	551,661,194	809,232,680	1,043,647,446	394,137,000	370,718,107	336,387,994	293,051,566	324,256,485
Tax					16,389,567	82,749,179	169,938,863	219,165,964	82,768,770	77,850,802	70,641,479	61,540,829	68,093,862
Tax rate					*5%*	*15%*	*21%*	*21%*	*21%*	*21%*	*21%*	*21%*	*21%*
Net income	(13,852,996)	(20,930,491)	(21,689,402)	30,896,518	311,401,780	468,912,015	639,293,817	824,481,483	311,368,230	292,867,304	265,746,515	231,510,737	256,162,623
Growth					*908%*	*51%*	*36%*	*29%*	*-62%*	*-6%*	*-9%*	*-13%*	*11%*
FCFE	(13,852,996)	(20,930,491)	(21,689,402)	30,896,518	311,401,780	468,912,015	639,293,817	824,481,483	311,368,230	292,867,304	265,746,515	231,510,737	256,162,623
Year	0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75
Discount rate	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*	*25%*
Discount factor	1.18	1.47	1.83	2.27	2.83	3.53	4.39	5.46	6.80	8.47	10.55	13.13	16.35
Discounted FCFE	**(11,753,486)**	**(14,263,728)**	**(11,872,218)**	**13,583,900**	**109,968,087**	**133,004,884**	**145,648,958**	**150,875,399**	**45,765,949**	**34,575,599**	**25,199,797**	**17,633,205**	**15,671,354**

Source: Aegis Capital estimates

Valuation	
Interim years	$654,037,702
Terminal value	$73,014,265
Implied value	$727,051,967

Value per share	**$6.02**

Source: Aegis Capital estimates

Fig. 11. Income statement

	FY:18A 3/31/2018	FY:19A 3/31/2019	1Q:20A 6/30/2019	2Q:20A 9/30/2019	3Q:20A 12/31/2019	4Q:20A 3/31/2020	FY:20A 3/31/2020	1Q:21A 6/30/2020	2Q:21E 9/30/2020	3Q:21E 12/31/2020	4Q:21E 3/31/2021	FY:21E 3/31/2021	1Q:22E 6/30/2021	2Q:22E 9/30/2021	3Q:22E 12/31/2021	4Q:22E 3/31/2022	FY:22E 3/31/2022
Revenue																	
Growth %																	
COGS																	
Gross profit																	
Gross margin %																	
Research and development	(7.8)	(17.1)	(4.3)	(4.2)	(3.0)	(1.8)	(13.4)	(1.7)	(1.9)	(2.1)	(2.3)	(8.0)	(2.9)	(3.3)	(3.8)	(4.4)	(14.4)
General and administrative	(6.4)	(7.5)	(1.9)	(1.1)	(2.9)	(1.4)	(7.4)	(1.4)	(1.4)	(1.5)	(1.5)	(5.8)	(1.6)	(1.6)	(1.7)	(1.7)	(6.5)
Total operating expenses	(14.2)	(24.6)	(6.2)	(5.4)	(6.0)	(3.3)	(20.8)	(3.1)	(3.3)	(3.6)	(3.8)	(13.9)	(4.4)	(4.9)	(5.5)	(6.1)	(20.9)
Gain (loss) from operations	(14.2)	(24.6)	(6.2)	(5.4)	(6.0)	(3.3)	(20.8)	(3.1)	(3.3)	(3.6)	(3.8)	(13.9)	(4.4)	(4.9)	(5.5)	(6.1)	(20.9)
EBIT margin %																	
Loss On Extinguishment Of Accounts Payable	(0.1)	(0.0)															
Other Income								0.0				0.0					
Gain (loss) before income taxes	(14.3)	(24.6)	(6.2)	(5.3)	(6.0)	(3.3)	(20.8)	(3.1)	(3.3)	(3.6)	(3.8)	(13.9)	(4.4)	(4.9)	(5.5)	(6.1)	(20.9)
Income Taxes																	
Tax rate %																	
Net Loss And Comprehensive Loss	(14.3)	(24.6)	(6.2)	(5.3)	(6.0)	(3.3)	(20.8)	(3.1)	(3.3)	(3.6)	(3.8)	(13.9)	(4.4)	(4.9)	(5.5)	(6.1)	(20.9)
Accrued Dividends On Series B Preferred Stock	(1.0)	(1.1)	(0.3)	(0.3)	(0.3)	(0.3)	(1.3)	(0.3)				(0.3)					
Deemed Dividend From Trigger Of Down Round Provision Feature	(0.2)	0.0															
Net income	(15.6)	(25.7)	(6.5)	(5.7)	(6.3)	(3.6)	(22.0)	(3.5)	(3.3)	(3.6)	(3.8)	(14.2)	(4.4)	(4.9)	(5.5)	(6.1)	(20.9)
Net margin %																	
EPS	**(1.12)**	**(0.90)**	**(0.15)**	**(0.13)**	**(0.15)**	**(0.08)**	**(0.50)**	**(0.07)**	**(0.04)**	**(0.04)**	**(0.04)**	**(0.19)**	**(0.05)**	**(0.05)**	**(0.05)**	**(0.06)**	**(0.22)**
Weighted average shares outstanding	*13.9*	*28.6*	*42.6*	*42.6*	*43.2*	*47.1*	*43.9*	*51.3*	*78.0*	*81.9*	*86.0*	*74.3*	*90.3*	*94.8*	*99.5*	*104.5*	*97.3*

Source: Company filings, Aegis Capital estimates, FactSet

Fig. 12. Historical financial highlights

Balance sheet highlights	
6/30 Cash and equivalents	$1.55mm
EverInsight Therapeutics PH94B license payment	$5.00mm
8/10 underwritten public offering	$14.29mm

Operating cash use	
FY:20 net cash used in operating activities	-$15.80mm
FY:19 net cash used in operating activities	-$14.50mm

Source: VistaGen

Sources

1. https://www.ncbi.nlm.nih.gov/pubmed/27561175
2. VistaGen
3. https://adaa.org/understanding-anxiety/social-anxiety-disorder
4. https://www.webmd.com/anxiety-panic/guide/mental-health-social-anxiety-disorder#1
5. https://www.nimh.nih.gov/health/publications/social-anxiety-disorder-more-than-just-shyness/index.shtml
6. https://adaa.org/resources-professionals/clinical-practice-review-social-anxiety#:~:text=Medications%20in%20these%20classes%20that,release%2C%20and%20venlafaxine%20extended%20release
7. https://www.mayoclinic.org/diseases-conditions/depression/symptoms-causes/syc-20356007
8. American Journal of Psychiatry 2014 171:675-682 (Liebowitz, et al)
9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5573566/
10. https://www.nimh.nih.gov/health/statistics/major-depression.shtml

Mentioned

Armour	Not rated
Echo	Not rated
Sontra	Not rated
Durham	Not rated
Morrison & Foerster	Not rated
SciClone	Not rated
Celerity	Not rated
Cato	Not rated
Excaliber	Not rated
Hayden	Not rated
MZ Group	Not rated
Artemis	Not rated
Progenitor	Not rated
Lineberger	Not rated
Basel Institute	Not rated
Calypte	Not rated
California & Hawaiian	Not rated
Discovery	Not rated
AstraZeneca	Not rated
Shire	Not rated
Alliance Advisors	Not rated
Stellar	Not rated

Required Disclosures

Price Target

Our PT on shares of VTGN is $6.00

Valuation Methodology

Our valuation methodology for shares of VTGN is a discounted cash flow analysis with a 25% discount rate.

Risk Factors

Clinical. VistaGen is a clinical-stage company. It is developing medicines. It's development-stage therapeutic candidates could fail in clinical trials. If this happens, it could have a significant adverse impact on the share price. There is a high failure rate, generally speaking, in biotechnology, and it has historically been difficult and costly to develop new medicines.
Financial. VistaGen does not have any revenue. It may never generate revenue. It has negative earnings and cash flow. This is associated with a higher risk profile.
Regulatory. Regulators, including but not limited to the FDA, could undertake decisions that could adversely impact the company's development efforts, and/or potential market entry, including blocking these altogether.
Dilution. VistaGen does not generate any revenue or cash flow. Therefore, it relies on external sources of financial (e.g. the capital markets). This is inherently a highly dilutive activity. Dilution could come from many sources and reduce the value of existing shareholders' equity claims.
Competition. There are many companies that are already selling treatments for the same indications that VistaGen is targeting. There are many others that are also developing new medicines. The competition could gain market share at VistaGen's expense.
COVID-19. Is a risk, including from business disruption.
Other externalities. Things could happen, external to and outside the control of the company, that could reduce value, and cause material declines in the share price
Analytical. We could have made errors in our analysis, or we could have neglected aspects of the story, or underappreciated the risks, all of which could make an equity investment in VTGN more risky than we presupposed and that could lead to losses.
Other. There are many risks, both known and unknown, all of which are serious.

For important disclosures go to www.aegiscap.com.

I, Nathan Weinstein, CFA, hereby certify that the views expressed in this research report accurately reflect my personal views about the subject companies and their securities. I also certify that I have not been, do not, and will not be receiving direct or indirect compensation in exchange for expressing the specific recommendations in this report.

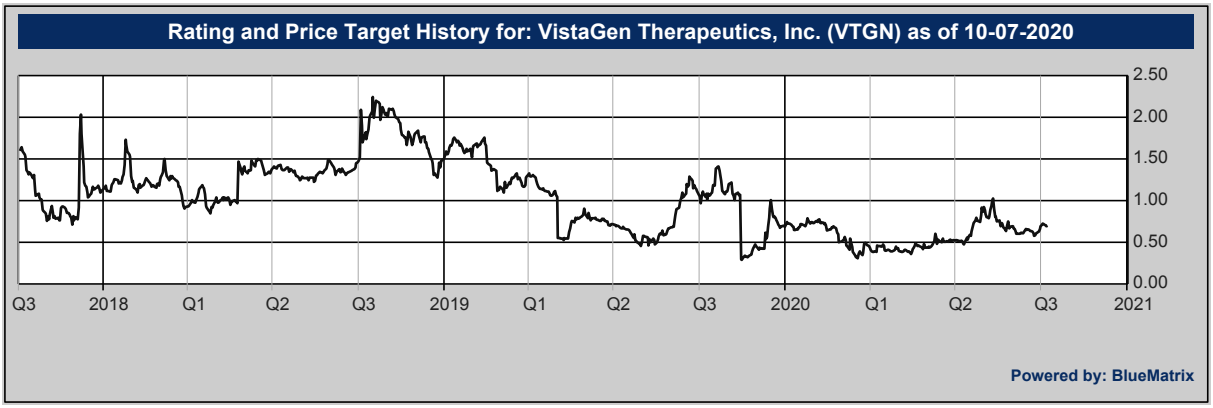
Research analyst compensation is not dependent upon investment banking revenues received by Aegis Capital Corp.

Aegis Capital Corp. intends to seek or expects to receive compensation for investment banking services from the subject company within the next three months.

The firm nor the Research Analyst have any material conflict of interest in which the Research Analyst has a reason to know or knows at the time of publication of this research report.

As of the report date neither Aegis Capital Corp. or its affiliates beneficially own 1% or more of any class of common equity securities of the subject company of this report.

Neither the research analyst who prepared this report or a member of the research analyst’s household has a financial position in the debt or equity securities of the subject company.



Rating	Percent	Investment Banking Services/Past 12 Mos. Percent
BUY [BUY]	91.30	38.10
HOLD [HOLD]	8.70	33.33
SELL [SELL]	0.00	0.00

Meaning of Ratings

A) A Buy rating is assigned when we do not believe the stock price adequately reflects a company's prospects over 12-18 months.

B) A Hold rating is assigned when we believe the stock price adequately reflects a company's prospects over 12-18 months.

C) A Sell rating is assigned when we believe the stock price more than adequately reflects a company's prospects over 12-18 months.

Other Disclosures

Other Disclosures The information contained herein is based upon sources believed to be reliable but is not guaranteed by us and is not considered to be all inclusive. It is not to be construed as an offer or the solicitation of an offer to sell or buy the securities mentioned herein. Aegis Capital Corp., its affiliates, shareholders, officers, staff, and/or members of their families, may have a position in the securities mentioned herein, and, before or after your receipt of this report, may make or recommend purchases and/or sales for their own accounts or for the accounts of other customers of the Firm from time to time in the open market or otherwise. Opinions expressed are our present opinions only and are subject to change without notice. Aegis Capital Corp. is under no obligation to provide updates to the opinions or information provided herein. Additional information is available upon request.

The common stock of the subject company in this report may not be suitable for certain investors based on their investment objectives, degree of risk, as well as their financial status.

Aegis Capital Corp.
(212) 813-1010
810 Seventh Avenue, 18th Floor
New York, New York 10019