Issuer Free Writing Prospectus
Filed Pursuant to Rule 433
Registration Statement No. 333-267206
(Preliminary Prospectus dated
October 6, 2022)

Corporate Overview

AVENUE THERAPEUTICS

AVENUE THERAPEUTICS, INC. | NASDAQ: ATXI | OCTOBER 2022

Notice & Disclaimers

Free Writing Prospectus
This free writing prospectus relates to the proposed public offering of securities of Avenue Therapeutics, Inc. (the "Company"), which is being registered with the U.S. Securities and Exchange Commission (the "SEC") on a Registration Statement on Form S-1 (No. 333-267206) (the as amended, "Registration Statement"). This free writing prospectus should be read together with the preliminary prospectus dated October 6, 2022 included within the Registration Statement pursuant to the Securities Act of 1933, as amended, which has preceded this free writing prospectus and can be accessed through the following link: https://www.sec.gov/Archives/edgar/data/1644963/000110465922105952/tm2224752d2_s1.htm.

The Company has filed a registration statement (including a preliminary prospectus) with the SEC for the offering to which this communication relates. Before you invest, you should read the registration statement (including the preliminary prospectus) and other documents the Company has filed with the SEC for more complete information about the Company and this offering. You may get these documents for free by visiting EDGAR on the SEC Web site at www.sec.gov or on the Company's Investor Relations website at http://ir.avenuetx.com. Alternatively, the Company, any underwriter or any dealer participating in the offering will arrange to send you the prospectus if you request it by calling the Prospectus Department at Aegis Capital Corp. at 1 (646) 502-2418.

Cautionary Note Regarding Forward-Looking Statements
This presentation contains predictive or "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of current or historical fact contained in this presentation, including statements that express our intentions, plans, objectives, beliefs, expectations, strategies, predictions or any other statements relating to our future activities or other future events or conditions are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "predict," "project," "will," "should," "would" and similar expressions are intended to identify forward-looking statements. These statements are based on current expectations, estimates and projections made by management about our business, our industry and other conditions affecting our financial condition, results of operations or business prospects. These statements are not guarantees of future performance and involve risks, uncertainties and assumptions that are difficult to predict. Therefore, actual outcomes and results may differ materially from what is expressed or forecasted in, or implied by, the forward-looking statements due to numerous risks and uncertainties. Factors that could cause such outcomes and results to differ include, but are not limited to, risks and uncertainties arising from: expectations for increases or decreases in expenses; expectations for the clinical and pre-clinical development, manufacturing, regulatory approval, and commercialization of our pharmaceutical product candidate or any other products we may acquire or in-license; our use of clinical research centers and other contractors; expectations for incurring capital expenditures to expand our research and development and manufacturing capabilities; expectations for generating revenue or becoming profitable on a sustained basis; expectations or ability to enter into marketing and other partnership agreements; expectations or ability to enter into product acquisition and in-licensing transactions; expectations or ability to build our own commercial infrastructure to manufacture, market and sell our product candidate; acceptance of our products by doctors, patients or payors; our ability to compete against other companies and research institutions; our ability to secure adequate protection for our intellectual property; our ability to attract and retain key personnel; availability of reimbursement for our products; estimates of the sufficiency of our existing cash and cash equivalents and investments to finance our operating requirements, including expectations regarding the value and liquidity of our investments; the volatility of our stock price; expected losses expectations for future capital requirements; uncertainty surrounding the Baergic Bio acquisition; and those risks discussed in our filings which we make with the SEC. Any forward-looking statements speak only as of the date on which they are made, and we undertake no obligation to publicly update or revise any forward-looking statements to reflect events or circumstances that may arise after the date of this presentation, except as required by applicable law. Investors should evaluate any statements made by us in light of these important factors.

Offering Summary

Issuer	Avenue Therapeutics, Inc.
Ticker / Exchange	NASDAQ / ATXI
Securities Offered	Common Stock and 100% Warrant Coverage
Offering Size	$12 million
Over-Allotment Option	15% of Offering
Use of Proceeds	$3 million of the net proceeds from this offering to repurchase all the shares of our Common Stock held by InvaGen under the terms of the Share Repurchase Agreement. Remainder of the net proceeds for general corporate purposes and working capital requirements, which may include, among other things, the advancement of BAER-101 and IV Tramadol.
Underwriter, Active Book-runner	Aegis Capital Corp.

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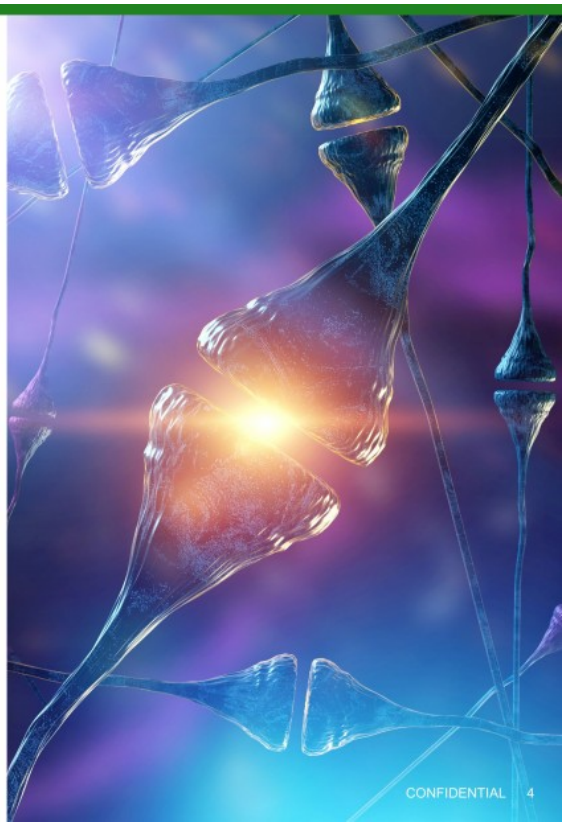
Executive Summary

- Avenue Therapeutics is a specialty pharmaceutical company that seeks to develop and commercialize therapies to treat central nervous system (CNS) conditions
- Our portfolio will soon include two clinical stage programs that we believe each have a significant market potential
  - **IV Tramadol** (Phase 3) for acute postoperative surgical pain
  - **BAER-101*** (Phase 1b) for epilepsy and acute anxiety
- Our clinical development programs are designed to meet near-term milestones that could build near-term value
- Potential to continue to expand pipeline through additional acquisitions in the rare / CNS disease space



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** Pending close of Share Contribution Agreement with Fortress Biotech, Inc. for Baergic Bio, Inc.*

Our clinical stage assets address large unmet patient and market needs in the CNS therapeutic space

Pipeline Asset	BAER-101*		IV Tramadol
Indication	Epilepsy and acute anxiety		Post operative pain
Mechanism	Selective GABA-A 2, 3 receptor positive allosteric modulator	+	Opioid agonist & inhibitor of norepinephrine & serotonin re-uptake
Key therapeutic value proposition	A safer and more tolerable benzodiazepine		Fills in the gap in acute care space between IV acetaminophen/NSAIDS and conventional narcotics
Comparable companies and transactions	Cerevel Therapeutics (Market cap ~$5B**)		Cadence Pharmaceuticals (acquired by Mallinckrodt for $1.4B in March 2014)

= Growing CNS portfolio

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*Note: * Contingent upon closing of the Baergic Bio acquisition; ** Market cap as of 9/8/22*

Our pipeline has near term value inflection points

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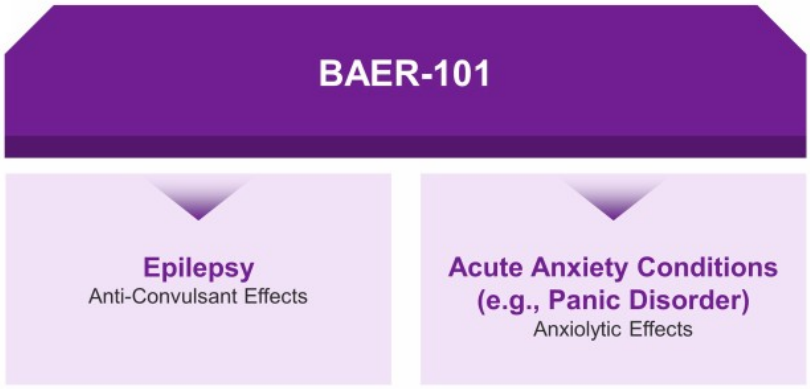
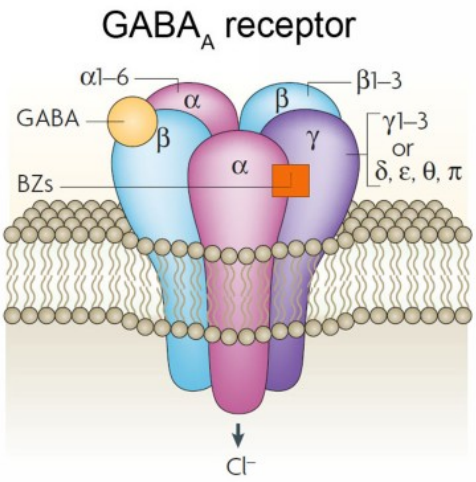
BAER-101 is being developed for epilepsy and acute anxiety



BAER-101 is a selective GABAα receptor agonist that produces anticonvulsant and anxiolytic activity



- GABA receptors are the major inhibitory neurotransmitter receptors in the mammalian brain
- GABA receptors have three major subunits α β γ, which are organized into a pentameric structure
- Each subunit has multiple subtypes (e.g., α1, α2, α3, α5) and these have different dominant functions

BAER-101 targets GABA α2 and α3 subtypes more than α1 and α5, which should have important clinical consequences

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Jacob et al., Nature Reviews Neuroscience, 2008

BAER-101 may have a more tolerable side effect profile compared to nonselective benzodiazepines due to greater GABA subtype selectively

Predicted effect of targeting GABA$_A$ subtypes

	Therapeutic Effect	GABA$_A$ subtypes			
		α1	α2	α3	α5
Positive	Anti-convulsant	✓✓	✓✓	✓✓	
Positive	Anxiolysis		✓✓	✓✓	
Positive	Analgesia		✓✓	✓	✓✓
Positive	Muscle Relaxation		✓✓	✓✓	
Negative	Sedation	✓✓			
Negative	Cognitive Impairment	✓✓			✓✓
Negative	Tolerance	✓✓			✓
Negative	Addiction	✓✓	✓		

Benzodiazepines

- Benzodiazepines (BZDs) are **non-selective** agonists of the alpha subunits α1, α2, α3 and α5
- BZDs have an extensive adverse event profile that can limit the dose and its effectiveness: somnolence, sedation, cognitive impairment, overuse, misuse and addiction

VS

BAER-101

- BAER-101 is a **selective agonist** at the α2 and α3 subunits
- The goal of BAER-101 is to provide anticonvulsant and anxiolytic activity by minimizing adverse events and risk of tolerance and abuse

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Epilepsy patients are prescribed benzodiazepines to control seizures, but have significant unmet needs for therapies with improved safety profiles

Disease

- **Epilepsy** is a chronic disease that manifests as recurrent seizures from abnormal electrical discharge in the brain
- Affects approximately 65M patients worldwide

Treatment

- Standard of care is the use of one or more anti-epileptic drugs (AED); Benzodiazepines (BZDs) are a class of AED that are used to treat seizures, but are generally not used as daily medication due to side effects

Unmet Need

- ~50% of epilepsy patients fail 1st line treatments and ~30% of patients are not well managed with any antiseizure medications
- BZDs are effective for seizures, but not well tolerated due to significant side effects including sedation, cognitive impairment, ataxia and can develop tolerance and addiction over time

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Source: CDC.gov; Kalilani L et al. The epidemiology of drug-resistant epilepsy: A systematic review and meta-analysis. Epilepsia. 2018 Dec

Acute anxiety patients also utilize benzodiazepines today and have significant unmet need for therapies with improved safety profiles

Disease

- **Panic disorder** is a common form of an **acute anxiety disorder** manifesting as frequent panic attacks unrelated to specific situations
- Manifests as intense episodes of apprehension, terror, feelings of impending doom and intense urge to flee
- Affects approximately 6.8M patients in the U.S.

Treatment

- Panic disorder is treated with a combination of cognitive behavioral therapy and benzodiazepines (BZDs), tricyclics, selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs)

Unmet Need

- BZDs are effective for panic disorder but not well tolerated due to sedation, cognitive impairment, ataxia and can develop tolerance and addiction over time

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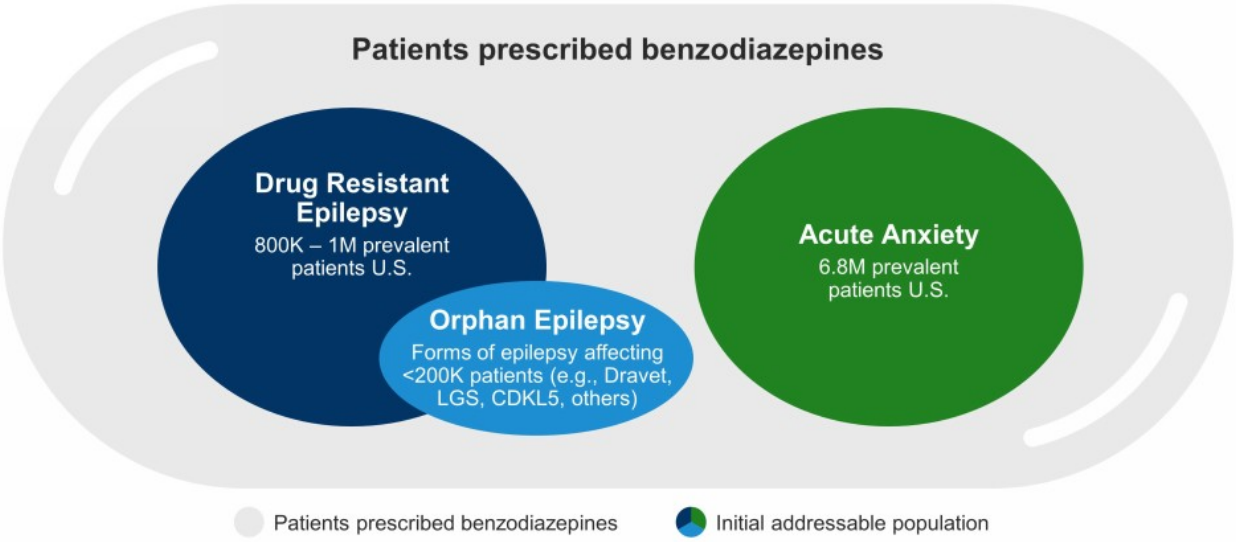
Source: ADAA.org

BAER-101 can target the large market of patients prescribed BZDs by targeting drug resistant epilepsy, orphan epilepsy, or acute anxiety

BAER-101 addressable market



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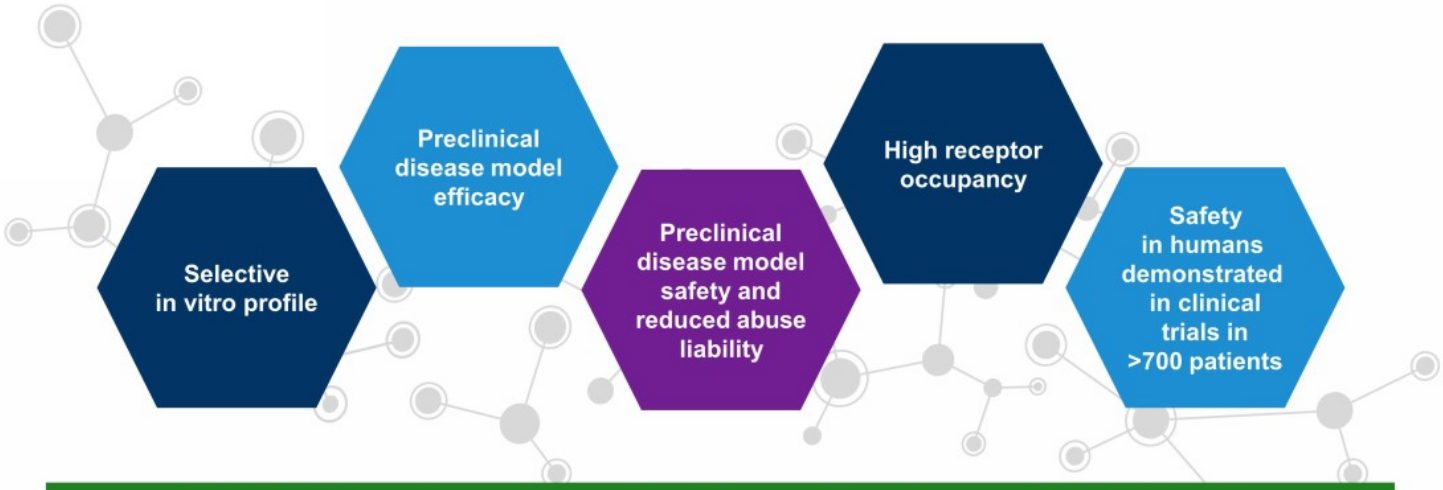
Source: CDC.gov; Grand View Research, Polaris Market Research; Kalilani L et al. The epidemiology of drug-resistant epilepsy: A systematic review and meta-analysis. Epilepsia. 2018 Dec; NORD; LGS Foundation; NIH.gov; ADAA.org

BAER-101 has a compelling profile to address this market



BAER-101 was licensed from AstraZeneca (where it was called AZD7325) in December 2019 with an extensive preclinical and clinical package

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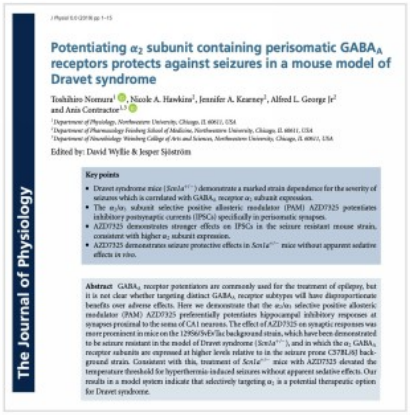
Preclinical in vivo studies demonstrate efficacy in multiple epilepsy models

Example: Dravet syndrome



The Journal of Physiology

Potentiating α_2 subunit containing perisomatic $GABA_A$ receptors protects against seizures in a mouse model of Dravet syndrome

Toshihiro Nomura[1], Nicole A. Hawkins[2], Jennifer A. Kearney[2], Alfred L. George Jr[2] and Anis Contractor[1,3]

[1] Department of Physiology, Northwestern University, Chicago, IL 60611, USA
[2] Department of Pharmacology Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, USA
[3] Department of Neurobiology Weinberg College of Arts and Sciences, Northwestern University, Chicago, IL 60611, USA

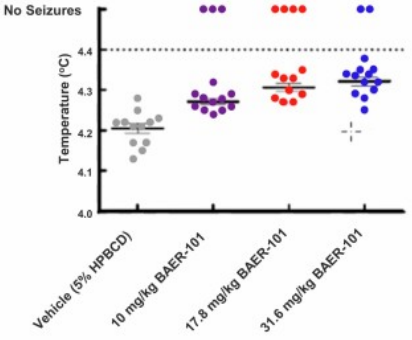
Edited by: David Wyllie & Jesper Sjöström

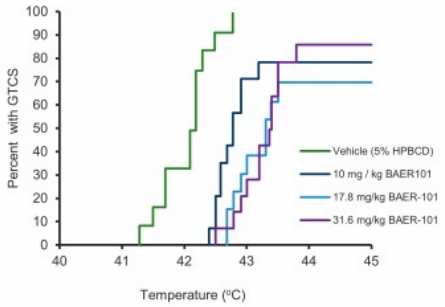
Key points

- Dravet syndrome mice (*Scn1a*$^{+/-}$) demonstrate a marked strain dependance for the severity of seizures which is correlated with $GABA_A$ receptor α_2 subunit expression.
- The $\alpha_2\beta_3$ subunit selective positive allosteric modulator (PAM) AZD7325 potentiates inhibitory postsynaptic currents (IPSCs) specifically in perisomatic synapses.
- AZD7325 demonstrates stronger effects on IPSCs in the seizure resistant mouse strain, consistent with higher α_2 subunit expression.
- AZD7325 demonstrates seizure protective effects in *Scn1a*$^{+/-}$ mice without apparent sedative effects in vivo.

Abstract GABA$_A$ receptor potentiators are commonly used for the treatment of epilepsy, but it is not clear whether targeting distinct GABA$_A$ receptor subtypes will have disproportionate benefits over adverse effects. Here we demonstrate that the $\alpha_2\beta3\gamma2$ selective positive allosteric modulator (PAM) AZD7325 preferentially potentiates hippocampal inhibitory responses at synapses proximal to the soma of CA1 neurons. The effect of AZD7325 on synaptic responses was more prominent in mice on the 129S6/SvEvTac background strain, which have been demonstrated to be seizure resistant in the model of Dravet syndrome (*Scn1a*$^{+/-}$), and in which the α_2 GABA$_A$ receptor subunits are expressed at higher levels relative to in the seizure prone C57BL/6J background strain. Consistent with this, treatment of *Scn1a*$^{+/-}$ mice with AZD7325 elevated the temperature threshold for hyperthermia-induced seizures without apparent sedative effects. Our results in a model system indicate that selectively targeting α_2 is a potential therapeutic option for Dravet syndrome.

BAER-101 decreases hyperthermia induced seizures in a mouse model of Dravet syndrome (SCN1A+/)





In a mouse model of Dravet syndrome BAER-101 was protective against seizures without notable sedation

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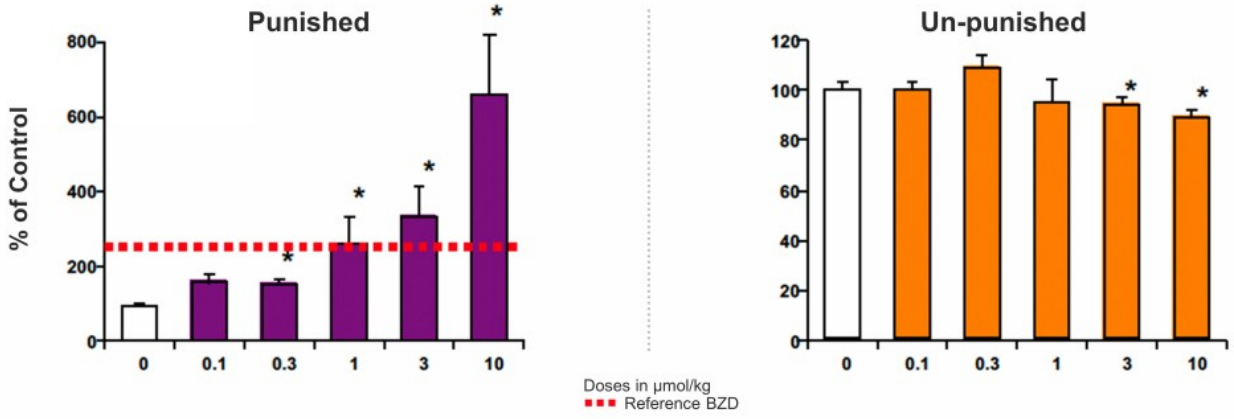
Note: BAER-101 was previously known as AZD7325 when tested in these preclinical models

Preclinical in vivo studies demonstrate efficacy in multiple anxiety models

EXAMPLE: BAER-101 results in rat punished responding model



In the rat punished responding model, BAER-101 demonstrated an anxiolytic effect similar to benzodiazepines but with reduced side effects

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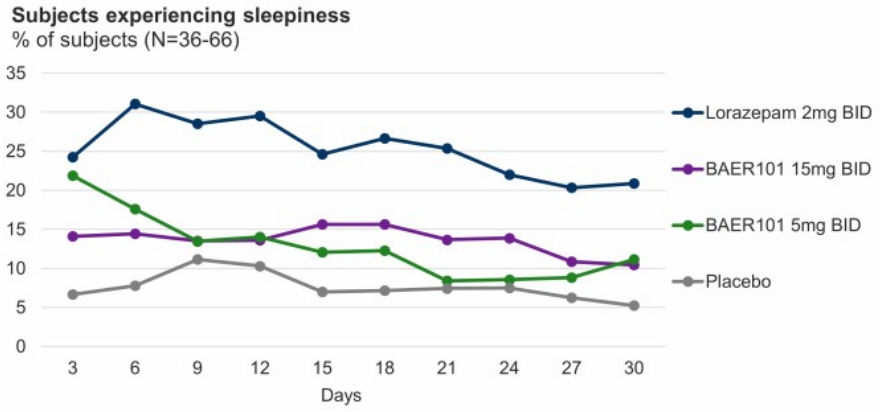
Note: BAER-101 was previously known as AZD7325 when tested in these preclinical models

AstraZeneca completed 10 clinical studies and demonstrated safety across trials

- BAER-101/AZD7325 was tested in over 700 subjects (healthy volunteers and patients)
- Side effects were mild or moderate with the most common side effects being dizziness and somnolence
- In two Phase 2 studies, BAER-101 was tested in patients with generalized anxiety disorder (GAD), but missed the primary endpoint
  - A sub analysis of the data with removal of dropouts and non-compliant patients (as measured by drug plasma levels), showed:
    - a dose-related anxiolytic signal
    - a correlation between average exposure and efficacy
  - Further, Cerevel's darigabat (a similar molecule) also missed the primary endpoint in the truncated GAD study and showed promising results in two Phase 1b studies in epilepsy and acute anxiety
- BAER-101 was also tested in a human abuse liability study where risk abuse with BAER-101 appeared lower than lorazepam (a BZD)

Clinical studies demonstrate positive sedation and cognition effects

Example: subset analysis from Phase 2 generalized anxiety study



Compared to the benzodiazepine lorazepam, two dosing regimens of BAER-101 led to less sedation as captured by the measurement of sleepiness

Note: BAER-101 was previously known as AZD7325 when tested in these preclinical models

We plan to initiate two Phase 1b studies that we expect to translate well into later development programs

Epilepsy: Photosensitivity Study

- The epilepsy photosensitivity model is a clinical translational model that provides proof-of-principle for antiepileptic activity in early clinical development
- Testing new antiepileptic drugs in this clinical model can provide data that translates well into larger and other epilepsy populations

WARNING!

The following contains bright, flashing lights and/or imagery that may cause discomfort and/or seizures for those with photosensitivity epilepsy.
Viewer discretion is advised.

Acute Anxiety: Hypercapnia CO2 Inhalation Model

- The CO2 inhalation challenge is a clinical translational model well-established in both healthy volunteers and in patients with panic disorder that provides proof-of-principle for anxiolytic activity in early clinical development
- The model is sensitive to drugs used to treat anxiety disorders (including benzodiazepines & SSRIs) and emerging new treatments with novel mechanisms

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BAER-101 is differentiated from others in the class

BAER-101 differentiation vs competitions

Company	Asset	Selectivity	Phase	Indications
Avenue Therapeutics	**BAER-101**	**α2/3-preferring**	**Phase 1**	**Epilepsy and panic disorder**
Cerevel (Nasdaq: CERE)	darigabat	α2/3/5-preferring	Phase 2	Epilepsy and panic disorder
Engrail Therapeutics	ENX101	α2/3/5-preferring	Phase 1b	Epilepsy
Saniona (OMX: Sanion)	SAN711	α3-preferring	Phase 1	Migraine and pain
RespireRx (OTC: RSPI)	KRM-II-81	α2/3-preferring	Preclinical	TBD

- BAER-101 is selective to the α2/3 receptor subunits and BAER-101 does not have high activity with the α5 subunit
- Furthest along GABAα compound in clinical development is darigabat from Cerevel, which targets the α5 subunit in addition to the α2/3 receptor subunits
  - Targeting the α5 receptor subunit is associated with tolerance development and this is potentially detrimental to developing a clinically effective drug for chronic use as resistance to the drug can occur over time. In addition, the α5 receptor subunit is also associated with sedation
  - BAER-101, unlike darigabat, is less likely to lead to treatment resistance and sedation

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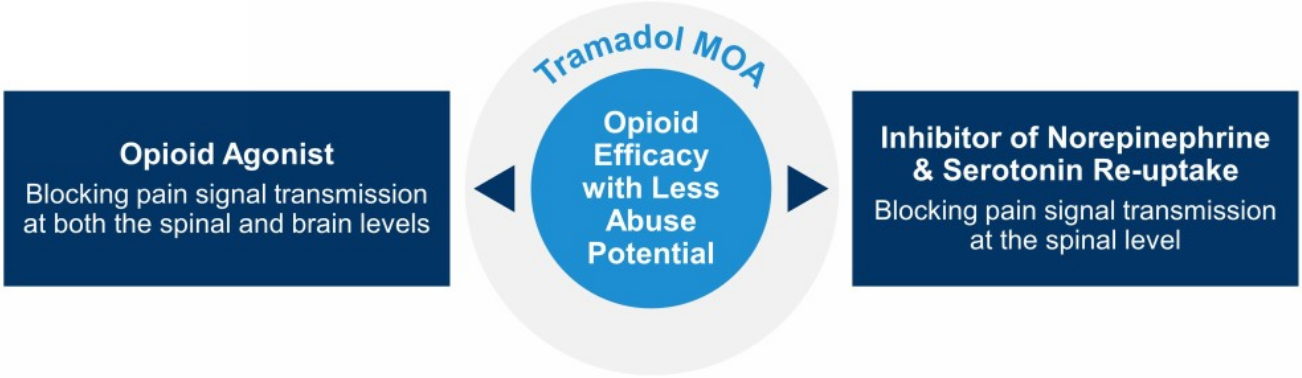
1 BAER-101

2 IV Tramadol

3 Acquire CNS / Rare Disease Assets

Tramadol has a unique dual mechanism of action among IV analgesics



Schedule IV versus Conventional Narcotics (Schedule II)

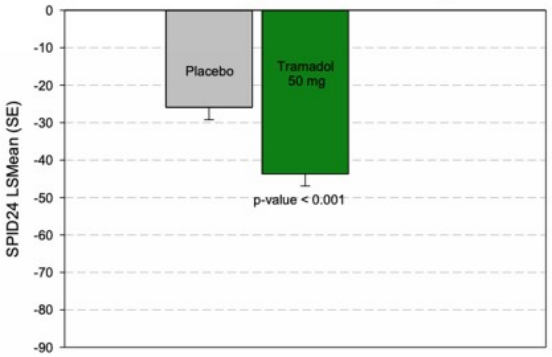
**IV Tramadol has been safely used in Europe for 30 years –
Approximately 370 million doses were administered in Europe from 2010 to 2019**

Note: Schedule IV means a low potential for abuse and low risk of dependence. Schedule II drugs have a high potential for abuse, with use potentially leading to severe psychological or physical dependence.
Source: https://www.dea.gov/druginfo/ds.shtml

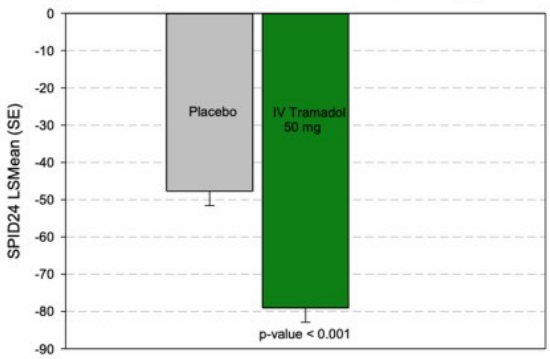
Safety and efficacy has been demonstrated in two Phase 3 trials in over 700 patients

Both pain relief study models show benefit of Tramadol over placebo

Study AVE-901-102 (Bunionectomy) SPID24



Study AVE-901-103 (Abdominoplasty) SPID24



p-value is comparing IV tramadol to placebo.

IV Tramadol 50 mg achieved primary endpoint and all key secondary endpoints

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Regulatory history and now a path forward for IV Tramadol NDA

2019

December 2019: We submitted a New Drug Application ("NDA") for IV Tramadol and received a Complete Response Letter (CRL) from the FDA in October 2020.

2021

February 2021: We addressed the manufacturing issue identified in the CRL and resubmitted the NDA for IV Tramadol.

June 14, 2021: We announced that we had received a second CRL from the FDA regarding our NDA for IV Tramadol. While efficacy and safety endpoints were met in clinical trials, the FDA expressed a desire for additional safety data related to opioid stacking, which was not directly addressed in the two Phase 3 trials.

2022

August 9, 2022: We met with the FDA to discuss a study design to address the agency's concern regarding opioid stacking, when rescue medicine is required in addition to IV tramadol, for patients with acute pain in the hospital monitored post surgical clinical setting.

We received the meeting minutes and the FDA stated that the proposed new study design appears reasonable and seems to address many of their concerns.

The Company intends to continue the dialogue with the FDA and submit a detailed protocol to gain alignment on a single safety study – the outcomes of this study could form the basis for resubmission of the NDA for IV tramadol

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Additional details on the history of regulatory interactions, decisions, and meetings between Avenue and the FDA are available in our public filings with the Securities and Exchange Commission

1 BAER-101

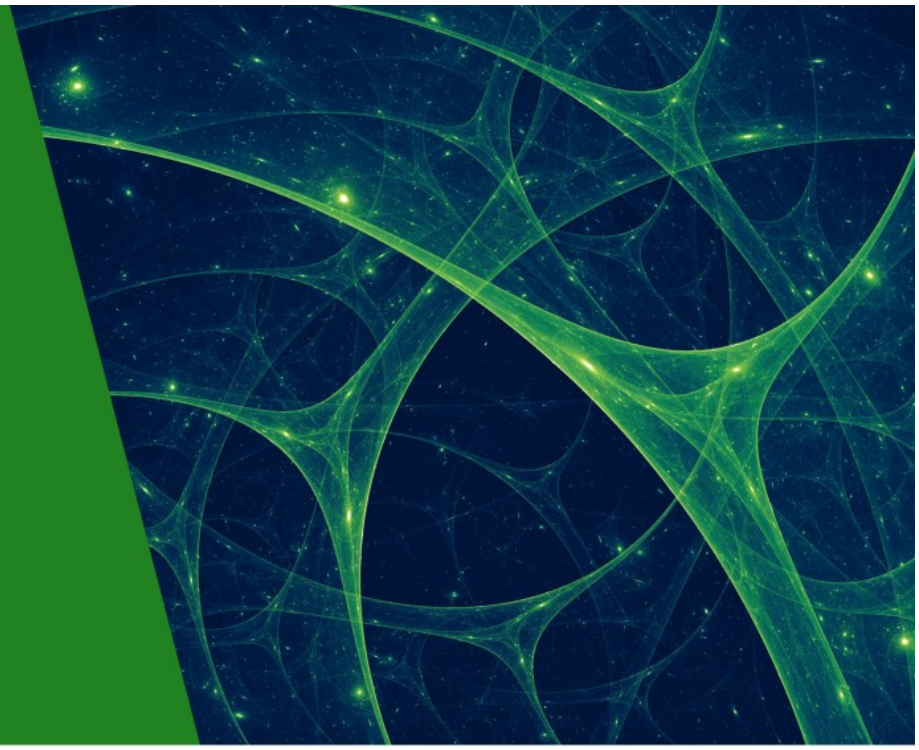
2 IV Tramadol

3 Acquire CNS / Rare Disease Assets

We are searching the world for first rate CNS / rare disease assets with these characteristics

- Imaging and Biomarker Driven Endpoints
- Feasible Clinical Development Programs with Reasonable Costs
- Clinical Stage with Human Data

Avenue Company Overview



We are led by an experienced management team and board of directors

Management

Alexandra MacLean MD
CEO

David Jin
Interim CFO

Michael Ryan
VP Clinical Operations & Program Management

Board of Directors

Lindsay Rosenwald MD
CEO, Fortress Biotech

Jay Kranzler MD PhD
Partner, Jay D Kranzler Consulting

Neil Herskowitz
Founder, ReGen Capital

Curtis Oltmans
Chief Legal Officer, Fulcrum Therapeutics

Faith Charles
Partner, Thompson Hine LLP

E. Garrett Ingram
President & CEO, Cipla Therapeutics, Inc.

Jaideep Gogtay, MD
CMO, Cipla Ltd.

IP / Exclusivity

BAER-101

- Two issued US patents and related foreign patents in European States (CH, DE, ES, FR, GB, IT and SE), China, Canada and Japan for composition of matter with expiry date of December 2026
  - Eligible for patent term extension (expected 5 years)
  - Potential for Orphan Drug Designation for rare epilepsies (7 years market exclusivity)
- Two issued US patents for method of use in a childhood development disorder with expiry date of January 2036
- Additional IP under development for specific indication needs

IV Tramadol

- Proprietary dosing regimen is patent-protected in the US until 2036, excluding patent term extension
- Portfolio also includes drug patents covering combinations

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- Our portfolio will soon include two clinical stage programs that we believe each have a significant market potential
  - **IV Tramadol** (Phase 3) for acute postoperative surgical pain
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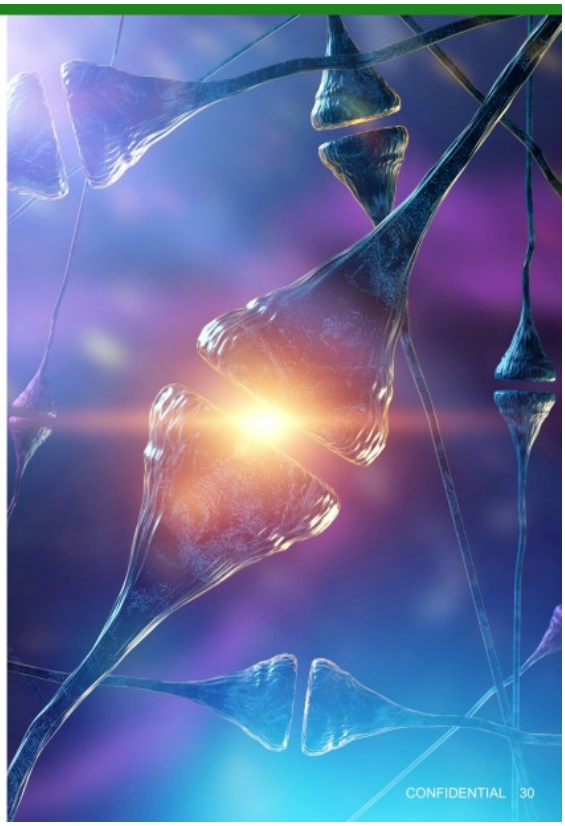
- Potential to continue to expand pipeline through additional acquisitions in the rare / CNS disease space



** Pending close of Share Contribution Agreement with Fortress Biotech, Inc. for Baergic Bio, Inc.*