Filed Pursuant to Rule 424(b)(3)
Registration No. 333-250964

PROSPECTUS SUPPLEMENT NO. 5
(to prospectus dated March 25, 2021)

Up to 42,437,330 Shares of Common Stock
166,333 Warrants to Purchase Common Stock

This prospectus supplement no. 5 (this "prospectus supplement") amends and supplements the prospectus dated March 25, 2021 (as supplemented or amended from time to time, the "Prospectus") which forms a part of our Registration Statement on Form S-1 (Registration Statement No. 333-250964). This prospectus supplement is being filed to update and supplement the information included or incorporated by reference in the Prospectus with the information contained in our Current Report on Form 8-K, filed with the Securities and Exchange Commission (the "SEC") on June 29, 2021 (the "Form 8-K"). Accordingly, we have attached the Form 8-K to this prospectus supplement.

This prospectus supplement updates and supplements the information in the Prospectus and is not complete without, and may not be delivered or utilized except in combination with, the Prospectus, including any amendments or supplements thereto. This prospectus supplement should be read in conjunction with the Prospectus and if there is any inconsistency between the information in the Prospectus and this prospectus supplement, you should rely on the information in this prospectus supplement.

Our common stock and warrants are listed on The Nasdaq Capital Market under the symbols "CERE" and "CEREW", respectively. On June 28, 2021, the closing price of our common stock was $12.57 per share and the closing price of our warrants was $3.87 per share.

Investing in our securities involves risks that are described in the "*Risk Factors*" section beginning on page 10 of the Prospectus.

Neither the SEC nor any state securities commission has approved or disapproved of the securities to be issued under the Prospectus or determined if the Prospectus or this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is June 29, 2021.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 29, 2021

CEREVEL THERAPEUTICS HOLDINGS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-39311**	**85-3911080**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

222 Jacobs Street, Suite 200
Cambridge, MA 02141
(Address of principal executive offices, including zip code)

(844) 304-2048
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.0001 per share	**CERE**	**The Nasdaq Capital Market**
Warrants to purchase one share of common stock at an exercise price of $11.50	**CEREW**	**The Nasdaq Capital Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On June 29, 2021, Cerevel Therapeutics Holdings, Inc. (the "Company") announced results from its Phase 1b clinical trial of CVL-231, a novel muscarinic M4-selective Positive Allosteric Modulator (PAM), in patients with schizophrenia. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information contained in Item 7.01 of this Current Report on Form 8-K and Exhibit 99.1 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01. Other Information.

On June 29, 2021, the Company also posted a corporate presentation on topline data from its Phase 1b clinical trial of CVL-231 for its investor call on its website. A copy of the corporate presentation is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1	Press Release issued by Cerevel Therapeutics Holdings, Inc., dated June 29, 2021
99.2	Corporate presentation of Cerevel Therapeutics Holdings, Inc., dated June 29, 2021

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

CEREVEL THERAPEUTICS HOLDINGS, INC.

Date: June 29, 2021

By: /s/ Scott Akamine
Scott Akamine
Chief Legal Officer & Secretary

Cerevel Therapeutics Announces Positive Topline Results for CVL-231 in Phase 1b Clinical Trial in Patients with Schizophrenia

Both doses of CVL-231 demonstrated a clinically meaningful and statistically significant improvement in PANSS Total score at 6 weeks and were overall well-tolerated compared with placebo

30 mg of CVL-231 once daily improved PANSS Total score at 6 weeks by 12.7 points compared with placebo (p=0.023)

20 mg of CVL-231 twice daily improved PANSS Total score at 6 weeks by 11.1 points compared with placebo (p=0.047)

No meaningful differences in gastrointestinal side effects, extrapyramidal symptoms or weight gain compared with placebo

Cerevel plans to advance CVL-231 to Phase 2 development in Schizophrenia and to evaluate the potential for this mechanism in other populations, including Dementia-Related Psychosis

Conference Call and Webcast scheduled for today at 8:30 a.m. EDT

CAMBRIDGE, Mass. – June 29, 2021 – Cerevel Therapeutics (Nasdaq: CERE), a company dedicated to unraveling the mysteries of the brain to treat neuroscience diseases, today announced positive results from its Phase 1b clinical trial of CVL-231, a novel muscarinic M4-selective Positive Allosteric Modulator (PAM), in adult patients with schizophrenia. CVL-231 was generally well-tolerated, and discontinuation rates were similar between CVL-231 and placebo in the six weeks of dosing, at 22% each. Importantly, both the 30 mg once daily and the 20 mg twice daily doses demonstrated clinically meaningful antipsychotic activity with an overall well-tolerated profile compared with placebo. The CVL-231 30 mg once daily dose resulted in a statistically significant and clinically meaningful mean reduction from baseline of 19.5 points in the Positive and Negative Syndrome Scale (PANSS) total score and a mean reduction of 12.7 points in PANSS versus the placebo group (p=0.023). The CVL-231 20 mg twice daily dose resulted in a statistically significant and clinically meaningful mean reduction from baseline of 17.9 points in PANSS total score and a mean reduction of 11.1 points in PANSS total score compared with the placebo group (p=0.047). These results were further supported by clinically meaningful reductions in the PANSS Positive and PANSS Negative subscales.

In the previously completed Part A multiple ascending dose (MAD) phase of this study, doses of 5 mg to 40 mg (administered as 20mg BID) were explored with up to 21 days of administration at target dosage. The Part A MAD safety and tolerability data were supportive of proceeding to 6 weeks of dosing in the subsequent Part B portion of the trial, which is being reported today.The Part B portion was designed, in part, to evaluate the tolerability and explore the antipsychotic potential of CVL-231 in patients by measuring the effect on PANSS with selected doses of 30 mg once-daily and 20 mg twice-daily.

“We believe these results are impressive and provide important evidence for the specific activation of the M4 receptor as a potential treatment approach for schizophrenia,” said Dr. John M. Kane, Professor and Chairman, Department of Psychiatry at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell. “By selectively targeting the M4 receptor, CVL-231 appears to have yielded a robust and clinically meaningful antipsychotic effect while avoiding

both the debilitating extrapyramidal side effects commonly seen with dopamine antagonists, as well as the serious gastrointestinal side effects that have limited non-selective muscarinic compounds in the past."

CVL-231 is an M4-selective PAM being developed as a potential treatment for schizophrenia. CVL-231 is designed as a once-daily medication that selectively targets activation of the M4 receptor in the brain to reduce dopaminergic activity without direct dopamine receptor antagonist activity. CVL-231 has the potential to be a first-in-class once-daily, M4-selective PAM that may provide antipsychotic activity without the need for titration while minimizing gastrointestinal, extrapyramidal, and metabolic side effects seen with other antipsychotic medications. By selectively targeting the M4 receptor, CVL-231 has the potential to avoid the serious gastrointestinal side effects that have commonly been associated with, and have hindered clinical development of, non-selective muscarinic agents.

"We are extremely encouraged with these results, which we believe support our hypothesis that a targeted muscarinic therapy that is highly selective for M4 receptors could deliver clinically meaningful benefit in the treatment of schizophrenia," said John Renger, Ph.D., chief scientific officer at Cerevel. "By developing a molecule that is several hundred times more selective for M4 receptors over M1, M2, M3, and M5 receptors, we are expanding our understanding of how to best leverage the potential of the muscarinic pathway to effectively treat individuals with schizophrenia, with fewer of the dose-limiting side effects that occur with currently available therapies."

CVL-231 was generally well tolerated in the clinical trial. The incidence of treatment emergent adverse events for both dose cohorts were similar to placebo, including heart rate and blood pressure increases. The adverse event (AE) of headache had the highest incidence of reporting across all treatment groups, with placebo at 26%, 30 mg once daily at 30%, and 26% for the 20 mg twice daily cohort. Additionally, the rate of nausea was similar between CVL-231 and placebo (4% for placebo and 7% for both 30 mg once-daily and 20 mg twice-daily groups) and rates of other gastrointestinal AEs were very low and similar to placebo. CVL-231 was not associated with a greater incidence of weight gain than placebo and no adverse events related to extrapyramidal symptoms were reported. Serious adverse events reported in the study included COVID-19, accidental overdose, and exacerbation of schizophrenia (one instance of each).

"Novel approaches for treating schizophrenia have been challenging to identify for decades, and patients and caregivers are seeking new therapies that avoid debilitating side effects that lead to poor compliance and relapse," said Raymond Sanchez, M.D., chief medical officer at Cerevel. "We are working to develop CVL-231 to be a once-daily formulation with improved tolerability, and without the need for titration, which could potentially improve adherence and improve the vicious cycle of relapse with the exacerbation of symptoms so often seen with this illness."

Pharmacodynamic Results Summary

Week 6 (Day 42)	Placebo (N=27)	CVL-231 30 mg QD (N=27)	CVL-231 20 mg BID (N=27)	Combined CVL-231 (N=54)
PANSS Total Score				
LS Mean Change from Baseline	-6.8	-19.5	-17.9	-18.7
Difference vs Placebo (p-value)		-12.7 p = 0.023	-11.1 p = 0.047	-11.9 p = 0.014
PANSS Positive Score				
LS Mean Change from Baseline	-2.5	-6.8	-4.9	-5.8
Difference vs Placebo (p-value)		-4.3 p = 0.016	-2.4 p = 0.166	-3.3 p=0.028
PANSS Negative Score				
LS Mean Change from Baseline	0.1	-3.0	-3.6	-3.3
Difference vs Placebo (p-value)		-3.1 p = 0.009	-3.7 p = 0.002	-3.4 p = 0.001

Additional data from the trial will be presented at an upcoming scientific meeting.

The results of this trial support the advancement of CVL-231 into a Phase 2 program in schizophrenia. Cerevel also plans to explore additional related indications including dementia-related psychosis

“Consistent with the scientific approach we have taken across our broad neuroscience, CVL-231 leverages our differentiated understanding of neurocircuitry and the power of targeted receptor selectivity in the development of innovative medicines for patients in need,” said Dr. Tony Coles, chairperson and chief executive officer of Cerevel. “We are extremely encouraged by the data from this trial and believe CVL-231 has the potential to be a truly transformative therapy in schizophrenia, a disease area that has not seen the significant advancement in therapies that patients and physicians have been seeking for decades. Today’s data readout marks an exciting and important milestone in our journey to become the premier neuroscience company.”

About the Trial

The Phase 1b clinical trial was a two-part multiple ascending dose (MAD) trial to evaluate the safety, tolerability, pharmacokinetics and preliminary pharmacodynamics of repeated daily doses of CVL-231 in patients with a primary diagnosis of schizophrenia per the DSM-V. In Part A, the objectives were to characterize physiological effects, identify any dose-limiting tolerability effects, and to identify the maximum tolerated dose of CVL-231 in patients with stable schizophrenia symptoms. In Part A, fifty patients across five CVL-231 cohorts were evaluated versus placebo, and the emerging data from Part A informed the doses and dosing schedules for Part B. Part B was a randomized, double-blind, three-arm, placebo-controlled trial with the objective of further evaluating safety, PK and preliminary PD. In Part B, 81 patients with baseline PANSS total scores of at least 80 and experiencing acute exacerbation of psychosis were randomized 1:1:1 to CVL-231 at a dose of 20 mg BID, 30 mg QD, or placebo for a total of 6 weeks. The trial was 59% powered to detect a 7 point difference from placebo on the PANSS total score. The measures used for evaluation included change from baseline in PANSS total score and subscales (negative, positive and general psychopathology), as well as other measures.

About Schizophrenia

Schizophrenia is a serious, complex and debilitating mental health disorder characterized by a constellation of symptoms, including delusions, hallucinations, disorganized speech or behavior, slowed speech and blunted affect. Schizophrenia is also often associated with significant cognitive impairment, which further limits a patient’s ability to be gainfully employed and maintain relationships. Diagnosis of schizophrenia is usually made in young adulthood and the

disease follows a chronic and indolent course characterized by periods of remission and relapse. Only 20% of patients report favorable treatment outcomes and medication adherence is poor, with a compliance rate of about 60% and a discontinuation rate of 74% within 18 months.[1,2] Patients who discontinue their medication suffer from high relapse rates of 77% at one year and 90% at two years.[3] People with schizophrenia have a 10 to 25-year reduction in life expectancy compared to the general population.[4] An estimated 20 million people worldwide suffer from schizophrenia.[5]

Conference Call Information

Cerevel will host a conference call and webcast today, June 29, at 8:30 a.m. EDT to discuss the results of the Phase 1b trial of CVL-231 in schizophrenia. To access the call, please dial 833-665-0655 (domestic) or 702-495-1044 (international) and refer to conference ID 9584017. The live webcast and accompanying slides can be accessed on the investor relations section of the Cerevel Therapeutics website here. A replay will be available in the same section of the company's website for approximately 90 days.

About Cerevel Therapeutics

Cerevel Therapeutics is dedicated to unraveling the mysteries of the brain to treat neuroscience diseases. The company is tackling diseases with a targeted approach to neuroscience that combines expertise in neurocircuitry with a focus on receptor selectivity. Cerevel Therapeutics has a diversified pipeline comprising five clinical-stage investigational therapies and several pre-clinical compounds with the potential to treat a range of neuroscience diseases, including Parkinson's, epilepsy, schizophrenia, and substance use disorder. Headquartered in Cambridge, Mass., Cerevel Therapeutics is advancing its current research and development programs while exploring new modalities through internal research efforts, external collaborations, or potential acquisitions. For more information, visit www.cerevel.com.

Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause actual results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this press release, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Forward-looking statements in this press release include, but are not limited to, statements about the advancement of CVL-231 into a Phase 2 program in schizophrenia and plans to explore additional related indications. We cannot assure you that the forward-looking statements in this press release will prove to be accurate. Furthermore, if the forward-looking statements prove to be inaccurate, the inaccuracy may be material. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties, including, among others: clinical trial results may not be favorable; uncertainties inherent in the product

development process (including with respect to the timing of results and whether such results will be predictive of future results); the impact of COVID-19 on the timing, progress and results of ongoing or planned clinical trials; other impacts of COVID-19, including operational disruptions or delays or to our ability to raise additional capital; whether and when, if at all, our product candidates will receive approval from the FDA or other regulatory authorities, and for which, if any, indications; competition from other biotechnology companies; uncertainties regarding intellectual property protection; and other risks identified in our SEC filings, including those under the heading "Risk Factors" in our Quarterly Report on Form 10-Q filed with the SEC on May 17, 2021 and our subsequent SEC filings. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The forward-looking statements in this press release represent our views as of the date of this press release. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this press release.

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Cerevel Therapeutics
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1 Patel, K. (2014). Schizophrenia: Overview and Treatment Options. *Pharmacy and Therapeutics*. Published. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4159061/

2 Higashi, K. (2013). Medication adherence in schizophrenia: factors influencing adherence and consequences of nonadherence, a systematic literature review. Psychopharmacology. Published. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3805432/

3 Zipursky, R. (2013). Risk of symptom recurrence with medication discontinuation in first-episode psychosis: a systematic review. Pub Med. Published. https://pubmed.ncbi.nlm.nih.gov/23972821/

4 World Health Organization. (n.d.). *Information sheet*. https://www.who.int/mental_health/management/info_sheet.pdf

5 Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. (2018). The Lancet. Published. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32279-7/fulltext

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Transforming the Possible in Neuroscience

Topline Data for Phase 1b Trial of CVL-231 in Schizophrenia

June 2021

Forward-Looking Statements

This presentation contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain.

Forward-looking statements in this presentation include, but are not limited to: statements about the potential attributes and benefits of our product candidates, including with respect to receptor subtype selectivity, activity, side effect and tolerability profile and relevant indications; the format and timing of our product development activities and clinical trials, including the design of clinical trials and the timing of initiation, completion and data readouts for clinical trials; statements about the advancement of CVL-231 into a Phase 2 program in schizophrenia and plans to explore additional related; the timing and outcome of IND submissions and other regulatory interactions; the ability to compete with other companies currently marketing or engaged in the development of treatments for relevant indications; the size and growth potential of the markets for product candidates and ability to serve those markets; the rate and degree of market acceptance of product candidates, if approved; the potential effects of the business combination; the amount and timing of payments we may receive pursuant to the tavapadon financing transaction; the sufficiency of our financial resources, including to fund the tavapadon Phase 3 development program through NDA submission and to allocate capital to earlier stage assets; and our cash runway.

We cannot assure you that the forward-looking statements in this presentation will prove to be accurate. Furthermore, if the forward-looking statements prove to be inaccurate, the inaccuracy may be material. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties, including, among others: that we may not realize the expected benefits of the financing transaction; that clinical trial results may not be favorable; uncertainties inherent in the product development process (including with respect to the timing of results and whether such results will be predictive of future results); the impact of COVID-19 on the timing, progress and results of ongoing or planned clinical trials; other impacts of COVID-19, including operational disruptions or delays or to our ability to raise additional capital; whether and when, if at all, our product candidates will receive approval from the FDA or other regulatory authorities, and for which, if any, indications; competition from other biotechnology companies; uncertainties regarding intellectual property protection; and other risks identified in our SEC filings, including those under the heading "Risk Factors" in our Quarterly Report on Form 10-Q filed with the SEC on May 17, 2021 and our subsequent SEC filings.

In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The forward-looking statements in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation.

Agenda

Introduction	**Matthew Calistri** *Vice President, Investor Relations*
Overview	**Tony Coles, M.D.** *Chairperson & Chief Executive Officer*
CVL-231 Background and MOA	**John Renger, Ph.D.** *Chief Scientific Officer*
Trial Design & Results	**Raymond Sanchez, M.D.** *Chief Medical Officer*
Q&A	*All*

Summary of Topline Results

- **Both doses of CVL-231 demonstrated clinically meaningful improvements in PANSS Total Score:**
  - 30 mg QD: -19.5 pts at week 6
  - 20 mg BID: -17.9 pts at week 6
- **Statistically significant difference in PANSS Total Score versus placebo***:
  - 30 mg QD: -12.7 pts (p=0.023) at week 6
  - 20 mg BID: -11.1 pts (p=0.047) at week 6
- **Clinically meaningful improvements in both PANSS Positive and PANSS Negative subscales**
- **Generally well-tolerated:**
  - Discontinuation rates similar between treatment and placebo (22% for each arm including placebo)
  - Not associated with extrapyramidal side effects or weight gain
  - Gastrointestinal (GI) side effects were infrequent and were similar between treatment and placebo
  - Serious adverse events included COVID-19, accidental overdose, and exacerbation of schizophrenia (one instance of each)
- **Data support advancing CVL-231 into Phase 2 program in schizophrenia and evaluating the potential for this mechanism in additional indications, including dementia-related psychosis**

*Trial originally designed to be 59% powered to detect 7 point difference in PANSS total score vs. placebo

Cerevel's M4 PAM is a Potential Next Generation Antipsychotic

M4 PAM (CVL-231)
Potential New Standard of Care

Opportunity for Innovation in Schizophrenia
Current Standard of Care Uses Same Mechanism of Action (MOA) as Therapies from the 1950s

Potential First-in-Class Therapy with Novel MOA

- M4 Selective
- Targeted Muscarinic Activity
- Improved Tolerability

Large Market

- ~20M Patients Worldwide
- >$9B Revenues in 2018
- ~3.5% Growth per year

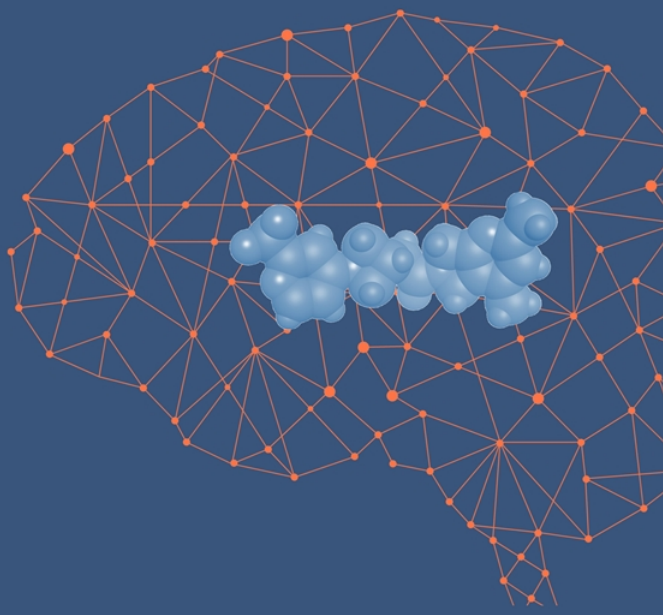
Significant Need for New Treatment Option

Debilitating side effects of atypicals often lead to discontinuation and relapse, driving a vicious cycle of disease progression

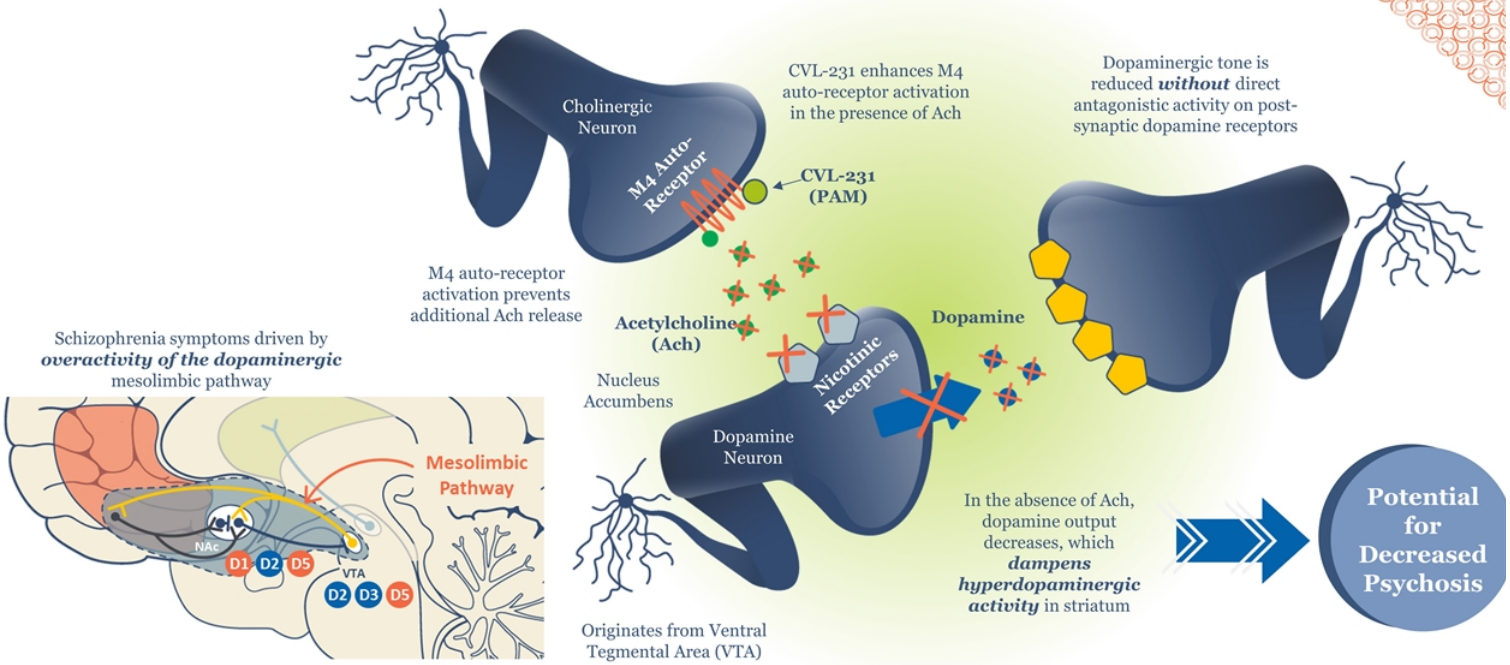
Source: World Health Organization, DRG Market Research, Global Data

Overview & Summary of CVL-231

CVL-231 is designed to be a novel once-daily treatment that selectively targets the M4 muscarinic receptor with the potential to provide antipsychotic activity while minimizing side effects



M4 Receptor Activation Reduces Dopamine in the Striatum



Schizophrenia symptoms driven by ***overactivity of the dopaminergic*** mesolimbic pathway

Cerevel's Selective M4 Modulation: A Compelling and Differentiated Approach to Drive Antipsychosis

M4 Selectively Impacts Brain Functions

Other Muscarinic Receptors	Potential Effect	M4 Muscarinic Receptor
-	Antipsychosis	✓✓
✓✓	Cognition	✓
✓✓	GI Side Effects	-
✓	Cardiovascular	✓

Receptor Subtype Selectivity Offers Potential Improvement

Xanomeline (M1/M4) data from Schizophrenia and Alzheimer's patients show targeting muscarinic receptor impacts brain function

But development limited by GI and CV side effects

Karuna's KarXT creatively addresses this by adding trospium to Xanomeline to offset side effects

Non-selective approach

M4 Knock-out mouse data suggests M4 receptors drive the antipsychotic activity of Xanomeline

M1 receptors believed to contribute to worrisome side effects

CVL-231:
Selective Potentially Once-daily M4 PAM

>600x
more selective for M4 over M1, 3 and 5

~360x
more selective than for M2

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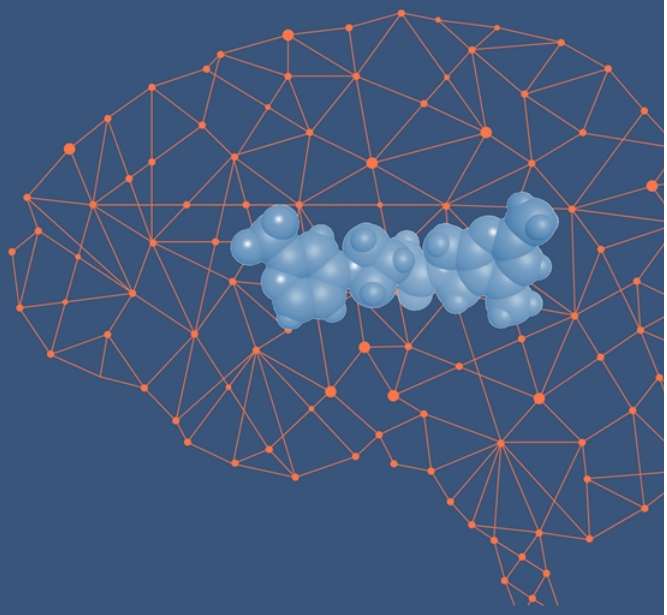
Source: 1. Shekhar et al. Am J Psychiatry, Vol 165, Aug 2008. N=20. 2 active and 3 placebo-arm patients discontinued the study, none due to adverse events.
2. Bodick et al. Arch Neurol, Vol 54, Apr 1997. N = 343. 52% of patients in high-dose arm discontinued treatment due to adverse events.

Trial Design & Results



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CVL-231 Phase 1b Trial Design

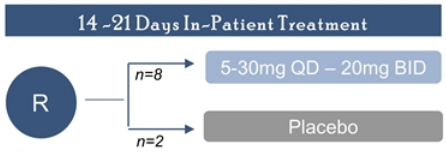
Part A: Safety Assessment

Multiple Ascending Dose

Primary Objective
- Safety & tolerability

Secondary Objective
- PK

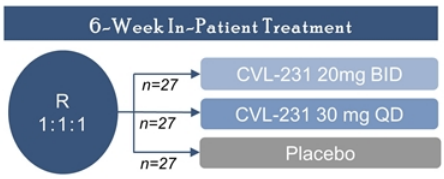
Up to 5 Cohorts (n=10 each)



Target Patient Population
- Male and female subjects, ages 18 to 50 years
- CGI-S ≤ 4 (normal to moderately ill) at screening and Day-1
- PANSS total score of ≤ 80 at the time of screening and Day-1

Part B: Pharmacodynamics

Exploratory PD Assessment
- Positive and Negative Syndrome Scale (PANSS)*
  - PANSS Positive Score
  - PANSS Negative Score
- Clinical Global Impression – Severity Scale (CGI-S)*
- Brief Assessment of Cognition in Schizophrenia (BACS) symbol coding test*



Target Patient Population
- Male and female subjects, ages 18 to 55 years
- PANSS total score of ≥80 at screening and Day -1
- CGI-S ≥4 (moderately to severely ill) at screening and Day -1
- History of relapse and/or exacerbation of symptoms when not receiving antipsychotic treatment, excluding the current episode
- Experiencing an acute exacerbation or relapse of symptoms, with onset less than 2 months prior to screening
- Population was enriched for key positive symptoms

* Trial not designed to demonstrate statistical significance

Phase 1b Part B: Demographics & Baseline Characteristics

	PBO N= 27	CVL-231 30 mg QD N= 27	CVL-231 20 mg BID N= 27	All CVL-231 N= 54	Total N= 81
Demographics					
Age (years) at Screening: Mean (SD)	41 (9.7)	41 (8.1)	38(9.8)	40(9.0)	40(9.2)
% Male: N (%)	19 (70%)	23 (85%)	21 (78%)	44 (81%)	63 (78%)
Race: N (%)					
Black or African American	17 (63%)	20 (74%)	19 (70%)	39 (72%)	56(69%)
White	9 (33%)	7 (26%)	7 (26%)	14 (26%)	23 (28%)
Other	1 (4%)	0	1 (4%)	1 (2%)	2 (2%)
Weight (kg) Prior to Dosing: Mean (SD)	90.0 (16.0)	85.4 (13.3)	85.4 (15.4)	85.4 (14.3)	86.9 (14.9)
Disease Characteristics at Baseline: Mean (SD)					
PANSS Total Score	93 (8.8)	93 (7.3)	97 (7.9)	95 (7.7)	95 (8.1)
PANSS Positive Score	24 (2.7)	25 (3.0)	26 (2.6)	26 (2.8)	25 (2.8)
PANSS Negative Score	23 (3.3)	22 (3.7)	24 (3.8)	23 (3.8)	23 (3.6)
CGI-S Score	5 (0.6)	5 (0.5)	5 (0.7)	5 (0.6)	5 (0.6)

Key Pharmacodynamic Assessments

Pharmacodynamic Results Summary*

Week 6 (Day 42)	Placebo N=27	CVL-231 30 mg QD N= 27	CVL-231 20 mg BID N= 27	Combined CVL-231 N=54
PANSS Total Score				
LS Mean Change from Baseline	-6.8	-19.5	-17.9	-18.7
Difference vs Placebo (p-value)†		-12.7†	-11.1†	-11.9†
		p = 0.023	p = 0.047	p = 0.014
PANSS Positive Score				
LS Mean Change from Baseline	-2.5	-6.8	-4.9	-5.8
Difference vs Placebo (p-value)		-4.3	-2.4	-3.3
		p = 0.016	p = 0.166	p = 0.028
PANSS Negative Score at Baseline				
LS Mean Change from Baseline	0.1	-3.0	-3.6	-3.3
Difference vs Placebo (p-value)		-3.1	-3.7	-3.4
		p = 0.009	p = 0.002	p = 0.001

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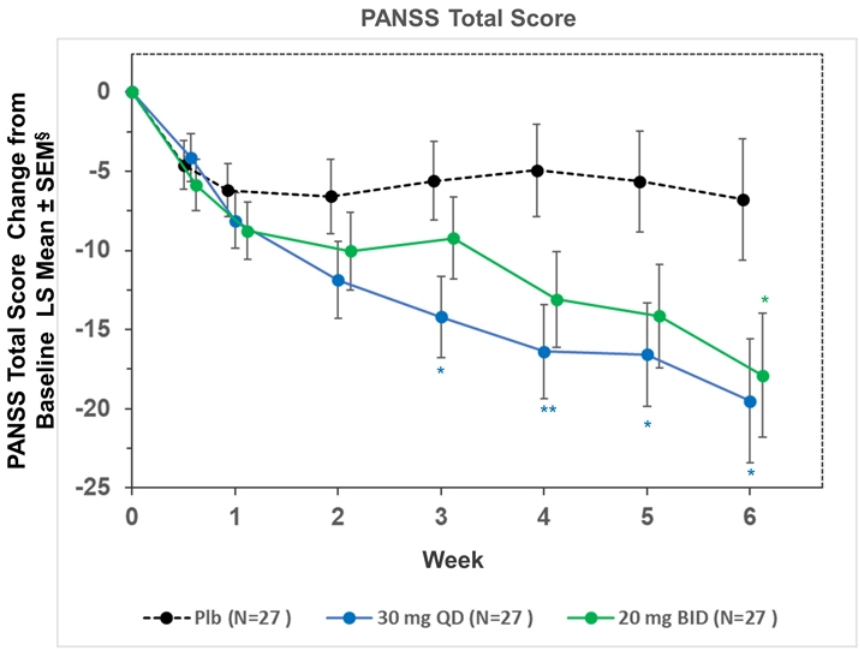
*Trial originally designed to be 59% powered to detect 7 point difference in PANSS total score vs. placebo
†Corresponds to Cohen's D effect sizes at Week 6 of -0.68 for CVL-231 30 mg QD, -0.59 for CVL-231 20 mg BID, and -0.64 for the two doses combined

Key Pharmacodynamic Endpoint – PANSS Total Score

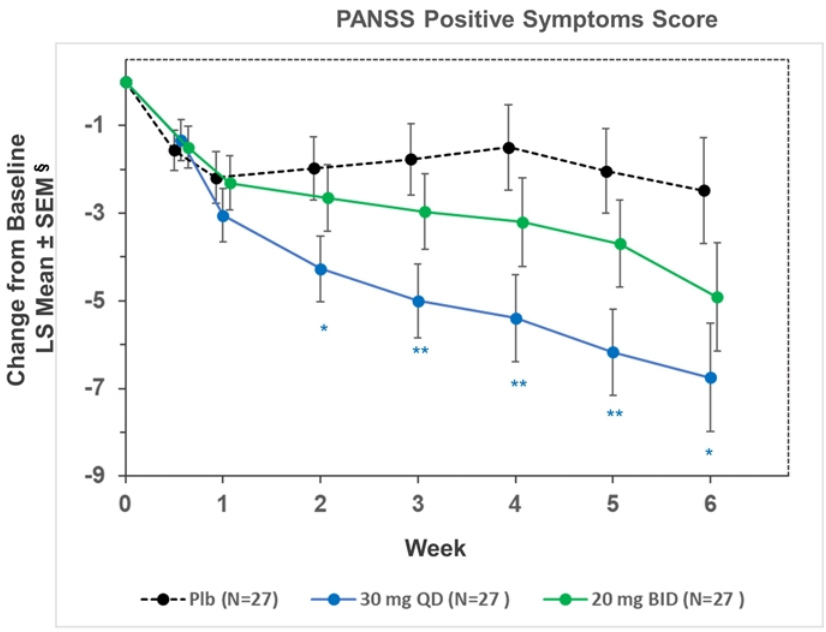


- 30 mg QD: 12.7 Point improvement versus placebo at Week 6 (19.5 of 30 mg QD vs 6.8 placebo) with P=0.023
- 20 mg BID: 11.1 Point improvement versus placebo at Week 6 (17.9 of 20 mg BID vs 6.8 placebo) with P=0.047
- Combined CVL 231: 11.9 Point improvement versus placebo at Week 6 (18.7 of CVL231 vs 6.8 placebo) with P=0.014

* P<0.05 vs Placebo ** P<0.01 vs Placebo

§ Derived from a mixed model for repeated measures (MMRM) with treatment group, visit, treatment group-by-visit interaction as fixed effect, baseline value as a covariate and the measurements within subject as repeated measures. An unstructured covariance matrix was used.

PANSS Positive Symptoms Score

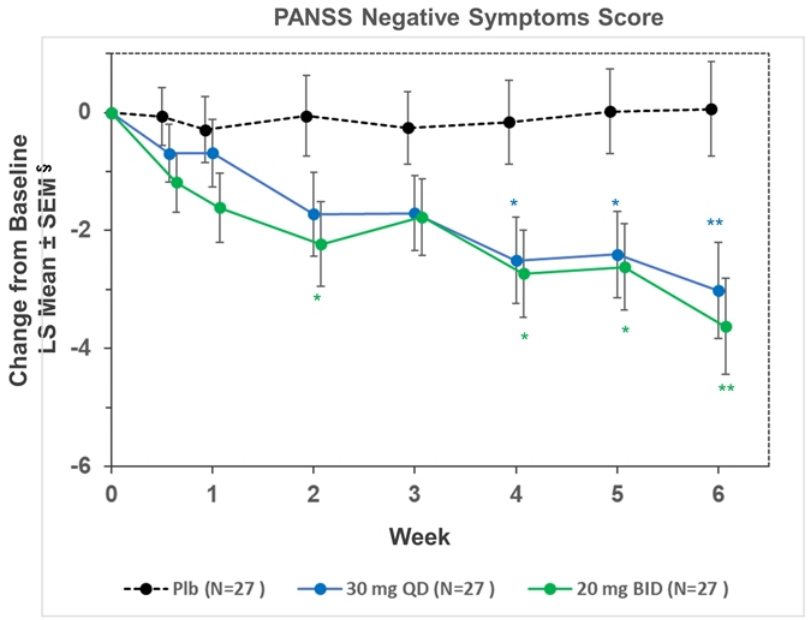


- 30 mg QD: 4.3 Point improvement versus placebo at Week 6 (6.8 of 30 mg QD vs 2.5 placebo) with P=0.016
- 20 mg BID: 2.4 Point improvement versus placebo at Week 6 (4.9 of 20 mg BID vs 2.5 placebo) with P=0.166
- Combined CVL 231: 3.3 Point improvement versus placebo at Week 6 (5.8 of CVL231 vs 2.5 placebo) with P=0.028

* P<0.05 vs Placebo ** P<0.01 vs Placebo

§ Derived from a mixed model for repeated measures (MMRM) with treatment group, visit, treatment group-by-visit interaction as fixed effect, baseline value as a covariate and the measurements within subject as repeated measures. An unstructured covariance matrix was used.

PANSS Negative Symptoms Score



- 30 mg QD: 3.1 Point improvement versus placebo at Week 6 (3.0 of 30 mg QD vs -0.1 placebo) with P=0.009
- 20 mg BID: 3.7 Point improvement versus placebo at Week 6 (3.6 of 20 mg BID vs -0.1 placebo) with P=0.002
- Combined CVL 231: 3.4 Point improvement versus placebo at Week 6 (3.3 of CVL231 vs -0.1 placebo) with P=0.001

* P<0.05 vs Placebo ** P<0.01 vs Placebo

§ Derived from a mixed model for repeated measures (MMRM) with treatment group, visit, treatment group-by-visit interaction as fixed effect, baseline value as a covariate and the measurements within subject as repeated measures. An unstructured covariance matrix was used.

Safety & Tolerability

Safety & Tolerability – Adverse Events

	PBO N= 27	CVL-231 30 mg QD N= 27	CVL-231 20 mg BID N= 27	All CVL-231 N= 54
Days on IMP				
Mean (SD)	37 (9.6)	36 (12.8)	35 (13.6)	36 (13.1)
Range	8, 42	4, 42	2, 42	2, 42
Number (%) Subjects with TEAE	14 (52%)	14 (52%)	15 (56%)	29 (54%)
Number (%) Subjects with TEAE Related to IMP	10 (37%)	7 (26%)	12 (44%)	19 (35%)
Number (%) Subjects with Serious TEAE	0	2 (7%)	1 (4%)	3 (6%)
Number (%) Subjects with AE of Special Interest (AESI)	3 (11%)	2 (7%)	4 (15%)	6 (11%)
Number (%) Subjects with TEAE Leading to Discontinuation of IMP	0	2 (7%)	1 (4%)	3 (6%)

Safety & Tolerability - Adverse Events

Incidences of All CVL-231 ≥ 2% and > Placebo

	PBO N= 27	CVL-231 30 mg QD N= 27	CVL-231 20 mg BID N= 27	All CVL-231 N= 54
Number (%) Subjects				
Headache	7 (26%)	8 (30%)	7 (26%)	15 (28%)
Nausea	1 (4%)	2 (7%)	2 (7%)	4 (7%)
Back pain	1 (4%)	2 (7%)	1 (4%)	3 (6%)
Blood creatine phosphokinase increased	0	1 (4%)	2 (7%)	3 (6%)
Dizziness	0	1 (4%)	2 (7%)	3 (6%)
Dry mouth	0	3 (11%)	0	3 (6%)
Somnolence	0	1 (4%)	2 (7%)	3 (6%)
Pruritus	0	1 (4%)	1 (4%)	2 (4%)

Safety & Tolerability

Serious AEs (SAEs) and AEs of Special Interest (AESIs)

	PBO N= 27	CVL-231 30 mg QD N= 27	CVL-231 20 mg BID N= 27	All CVL-231 N= 54
Number (%) Subjects with SAE				
COVID-19	0	0	1 (4%)	1 (2%)
Accidental overdose**	0	1 (4%)	0	1 (2%)
Schizophrenia**	0	1 (4%)	0	1 (2%)
Number (%) Subjects with AESI*				
Blood pressure increased	2 (7%)	0	0	0
Heart rate increased	1 (4%)	0	1 (4%)	1 (2%)
Blood pressure diastolic increased	0	0	1 (4%)	1 (2%)
Sinus tachycardia	0	0	1 (4%)	1 (2%)
Psychotic disorder**	0	0	1 (4%)	1 (2%)
Schizophrenia**	0	1 (4%)	0	1 (2%)
Accidental overdose**	0	1 (4%)	0	1 (2%)

***AEs leading to discontinuation of treatment with IMP. No other AE leading to discontinuation of IMP*

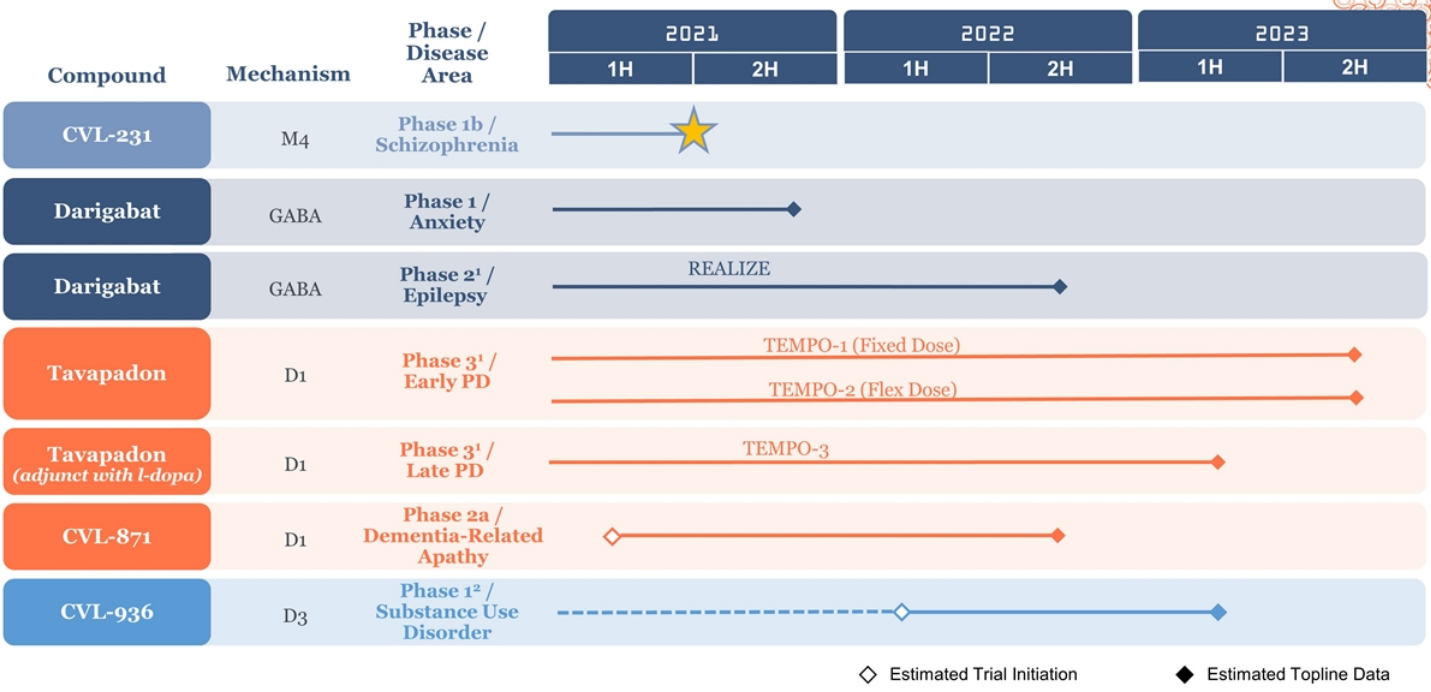
* AESIs specified in the protocol include 1. AEs that result in the discontinuation of treatment with IMP, 2. events that satisfy the criteria for suspected Hy's Law (ALT or AST >3 × ULN, AND serum bilirubin ≥2 × ULN, AND alkaline phosphatase <2 × ULN), 3. events of heart rate >120 bpm, and confirmed by ECG, 4. events of confirmed QTcF is >500 msec or the increase from baseline is >75 msec in subjects without significant hypokalemia, 5. events of mean triplicate blood pressure reading >160 mmHg systolic or >100 mmHg diastolic with confirmation.

Summary of Topline Results

- **Both doses of CVL-231 demonstrated clinically meaningful improvements in PANSS Total Score:**
  - 30 mg QD: -19.5 pts at week 6
  - 20 mg BID: -17.9 pts at week 6
- **Statistically significant difference in PANSS Total Score versus placebo***:
  - 30 mg QD: -12.7 pts (p=0.023) at week 6
  - 20 mg BID: -11.1 pts (p=0.047) at week 6
- **Clinically meaningful improvements in both PANSS Positive and PANSS Negative subscales**
- **Generally well-tolerated:**
  - Discontinuation rates similar between treatment and placebo (22% for each arm including placebo)
  - Not associated with extrapyramidal side effects or weight gain
  - Gastrointestinal (GI) side effects were infrequent and were similar between treatment and placebo
  - Serious adverse events included COVID-19, accidental overdose, and exacerbation of schizophrenia (one instance of each)
- **Data support advancing CVL-231 into Phase 2 program in schizophrenia and evaluating the potential for this mechanism in additional indications, including dementia-related psychosis**

*Trial originally designed to be 59% powered to detect 7 point difference in PANSS total score vs. placebo

Multiple Milestones Expected Over Next Three Years



1. In addition, there are two open-label extension trials ongoing (REALIZE OLE for darigabat in epilepsy and TEMPO-4 for tavapadon)
2. We initiated a Phase 1 SAD trial for CVL-936 in January 2020. We concluded dosing of Cohort 1 of the Phase 1 SAD trial. We intend to conduct a multiple dose canine EEG study prior to resuming Phase 1 SAD and MAD evaluations.