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Transforming the Possible in Neuroscience

Virtual R&D Event

October 7, 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 our Phase 2a trial for CVL-871, our Phase 2 program for CVL-231 and other statements regarding the design of clinical trials and the timing of initiation, completion and data readouts for clinical trials; the timing and outcome of 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; and the rate and degree of market acceptance of product candidates, if approved.

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 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 Annual Report on Form 10-Q filed with the SEC on August 11, 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.

Cerevel:
Transforming the Possible in Neuroscience

Who We Are is in Our Name

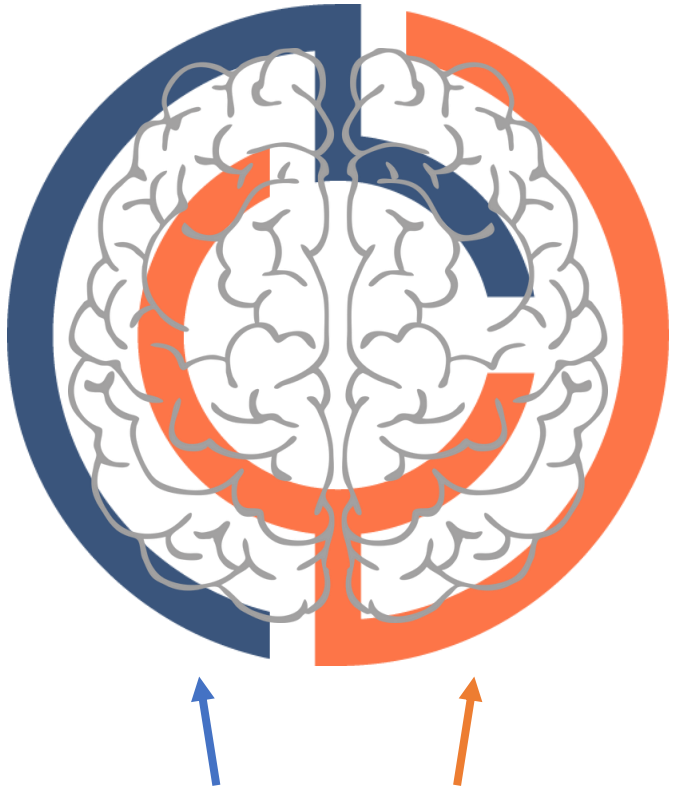
cerevel

cere = cerebrum

revel = revelation/reveal

We are bold thinkers, deep experts, resilient pathfinders, and transparent partners who push the boundaries of scientific understanding to unlock breakthrough CNS therapies that could have real impact on people's lives.

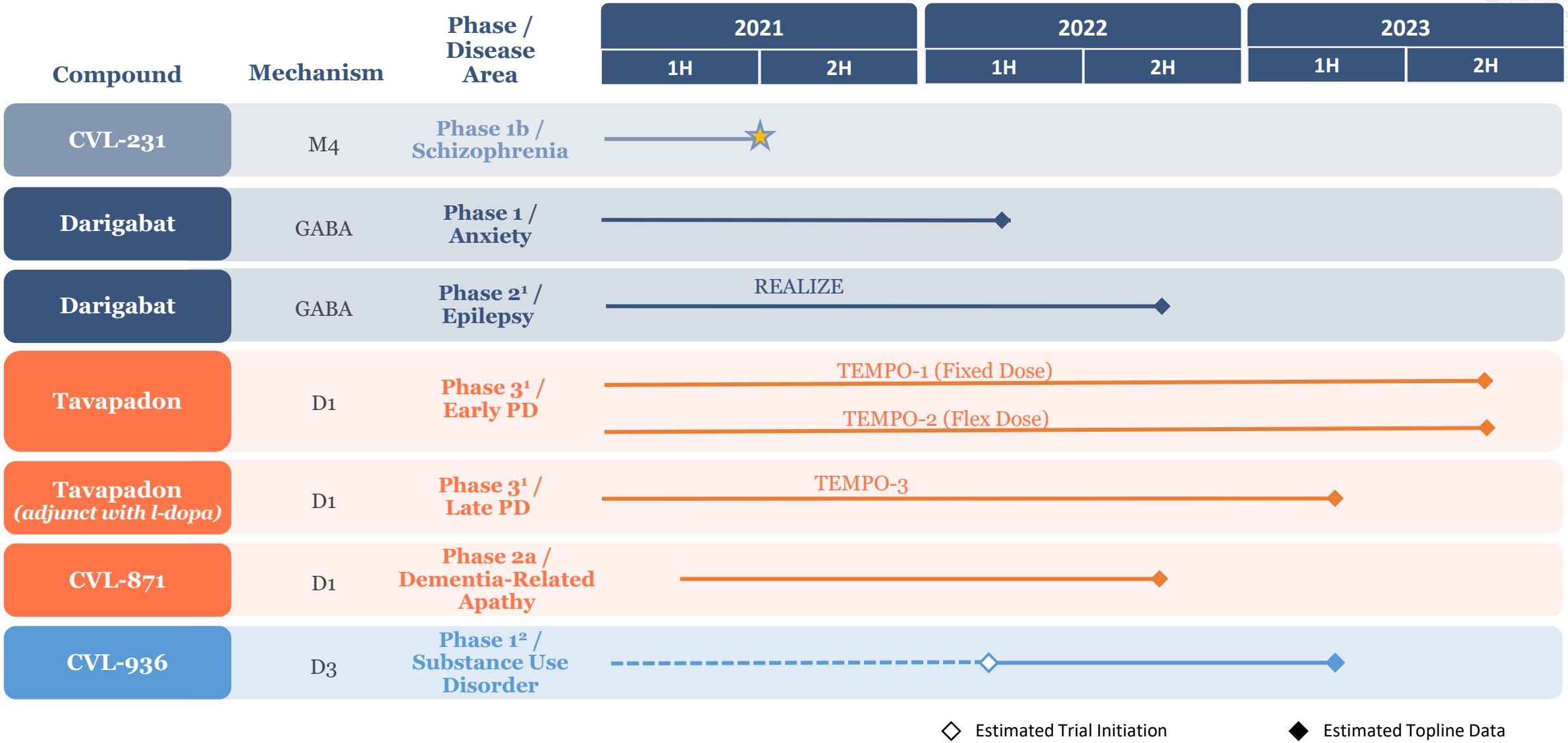
Brain hemispheres



Lock in key

Selective / Targeted Mechanisms

Multiple Milestones Expected Over Next Three Years



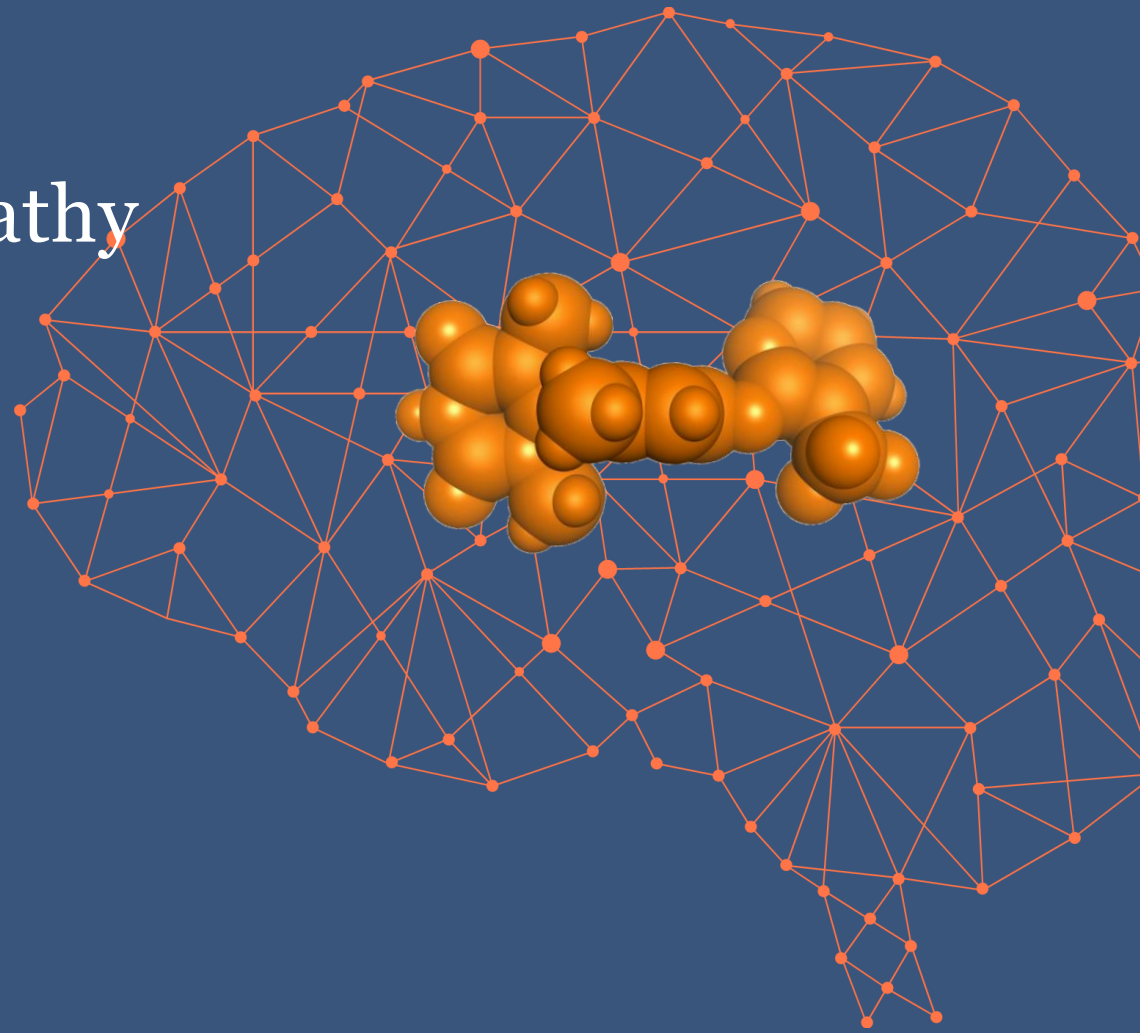
1. In addition, there are two open-label extension trials ongoing (REALIZE OLE for darigabat in epilepsy and TEMPO-4 for tavapadon)
2. We initiated a Phase 1 SAD trial for CVL-936 in January 2020. We concluded dosing of Cohort 1 of the Phase 1 SAD trial. We intend to conduct a multiple dose non-clinical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

Today's Agenda

Time	Topic	Presenter(s)
10:00 – 10:05	Cerevel: Transforming the Possible in Neuroscience	 **Tony Coles, M.D.** *Chief Executive Officer & Chairperson*
10:05 – 10:45	Deep Dive: CVL-871: D1/5 Partial Agonist for Dementia-Related Apathy	 **Raymond Sanchez, M.D.** *Chief Medical Officer*  **David Gray, Ph.D.** *VP, Chemistry*  **Matthew Leoni, M.D., M.B.A.** *VP, Global Clin. Development*
10:45 – 11:00	Dementia-Related Apathy: A Clinical Perspective	 **Krista Lanctôt, Ph.D.** *Professor of Psychiatry & Pharmacology/Toxicology, University of Toronto*
11:00 – 11:15	CVL-231: M4 PAM for Schizophrenia	 **John Renger, Ph.D.** *Chief Scientific Officer*  **Matthew Leoni, M.D.** *VP, Global Clin. Development*  **Sridhar Duvvuri, Ph.D.** *VP, Clin. Pharmacology & Pharmacometrics*
11:15 – End	Concluding Remarks / Q&A	All

CVL-871 in Dementia-Related Apathy

Partial agonist selectively targeting the dopamine D1 receptor with the goal of modulating motivation and reward pathways to address apathy in patients with mild-to-moderate dementia



Dementia-Related Apathy: A Patient's Perspective

High Unmet Need in Apathy, Which Affects ~50% of Patients with Dementia[1]

What is Apathy?

Leading neuropsychiatric symptom in dementia

Social disengagement and loss of emotion leads to:

- Impaired decision-making
- Lack of empathy, affection, or concern
- Loss of interest in personal well-being and relationships
- Inability to initiate and maintain normal daily activities
- Interference with basic functions*

CVL-871: Potential to be the First Treatment for Dementia-Related Apathy

High Unmet Need

- >50M Dementia Patients Worldwide[2]
- >3x Mortality Risk[3]
- Among strongest predictors of disease progression[4]
- Early institutionalization & ↑ caregiver burden[4]

No Approved Treatment

Off-label Use of…

Acetylcholinesterase Inhibitors	No proven effect in clinical trials
SSRIs/SNRIs	No established benefit May worsen apathy symptoms
Methylphenidate	Schedule II stimulant with CV risk in elderly patients

Sources: 1. Zhao, et al. J Affect Disord 2016. 2. ADI, 2015. 3. Linde, et al. Intl Journ Geriatric Psych 2016 4. Lanctôt et al 2017, Onyike et al 2007, Hongisto et al 2018, Lyketsos et al 2002. Bionest Research, May 2020.
*Including personal hygiene, eating, dressing, taking medication

CVL-871 Speaker Bios

David Gray, Ph.D.
Vice President, Chemistry

- Joined Cerevel October 2018
- 16 years in leadership roles at Pfizer
- Ph.D. in Organic Chemistry, Scripps Research Institute

Matthew Leoni, M.D., M.B.A.
Vice President, Global Clinical Development

- Joined Cerevel March 2019
- 13 years of clinical development experience at Galderma, Novartis & Otsuka
- M.D. from University of Pennsylvania, M.B.A. from Drexel University

CVL-871 Mechanism of Action

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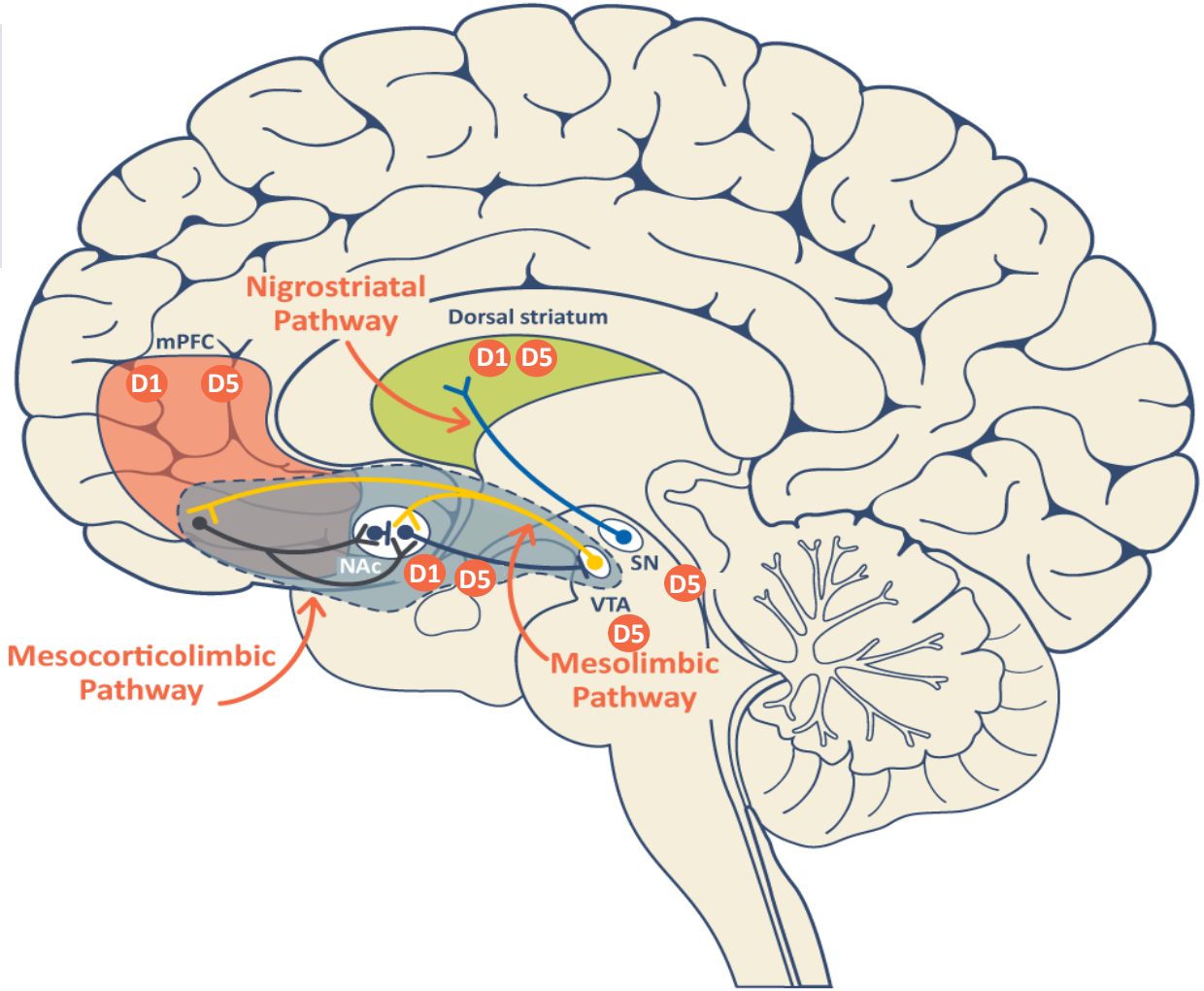
Dopamine is a Major Regulator in Multiple Distinct Circuits

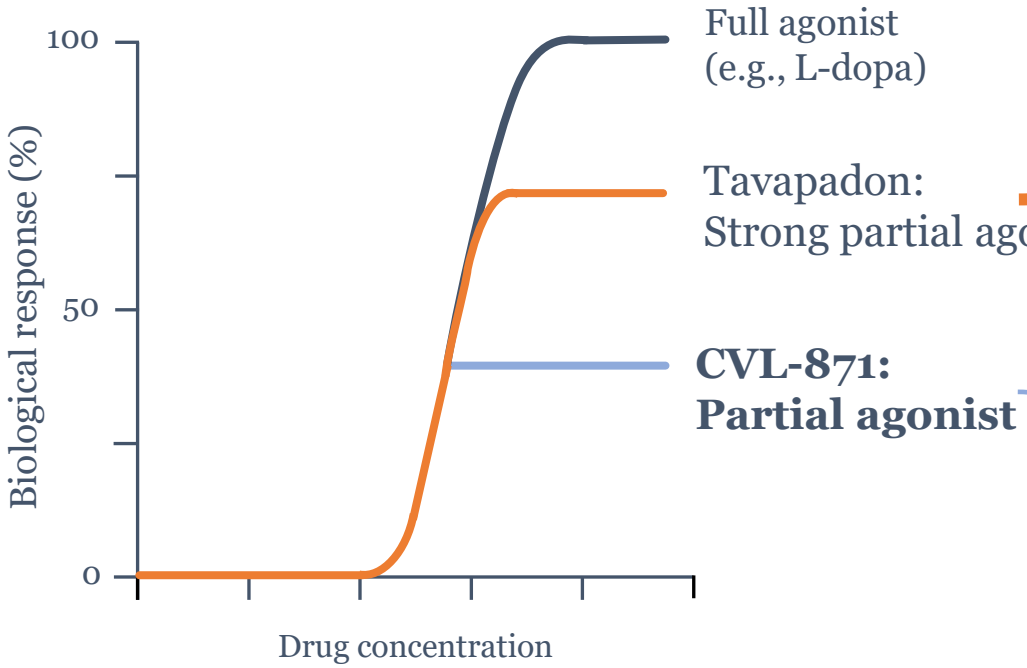
Motor function is mediated by the **nigrostriatal** dopamine circuit



Conscious ***goal-directed behavior & motivation*** are mediated by the **mesocorticolimbic** dopamine circuit

D1/D5 Partial Agonism to Address Motivation & Reward

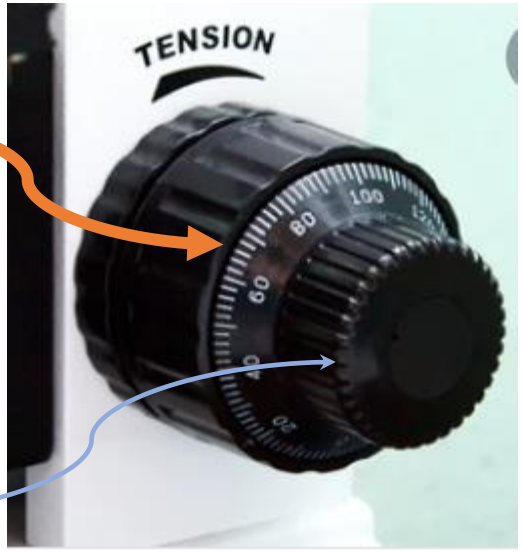
Degrees of Agonism (Illustrative)



Treating Apathy Requires Fine Adjustment to Dopaminergic Tone

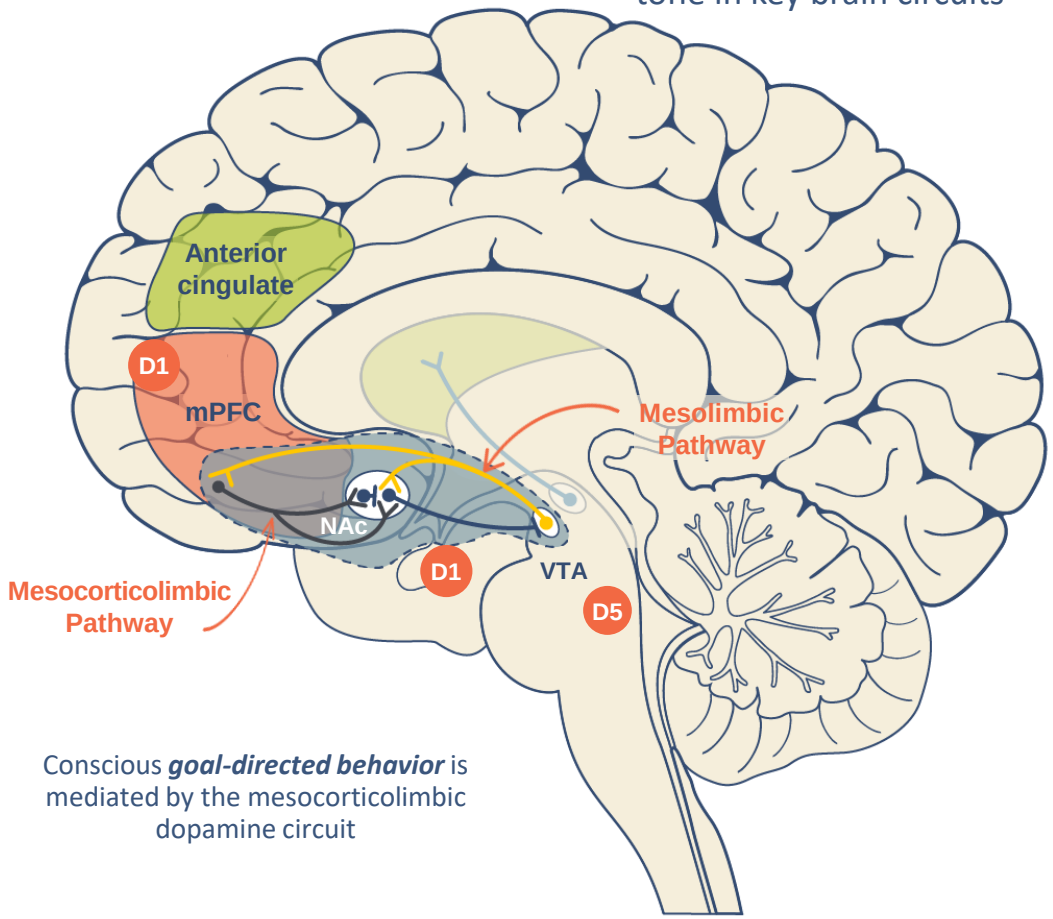
Coarse adjustment to address motor function deficit in Parkinson's

Fine adjustment to address motivation and reward in apathy

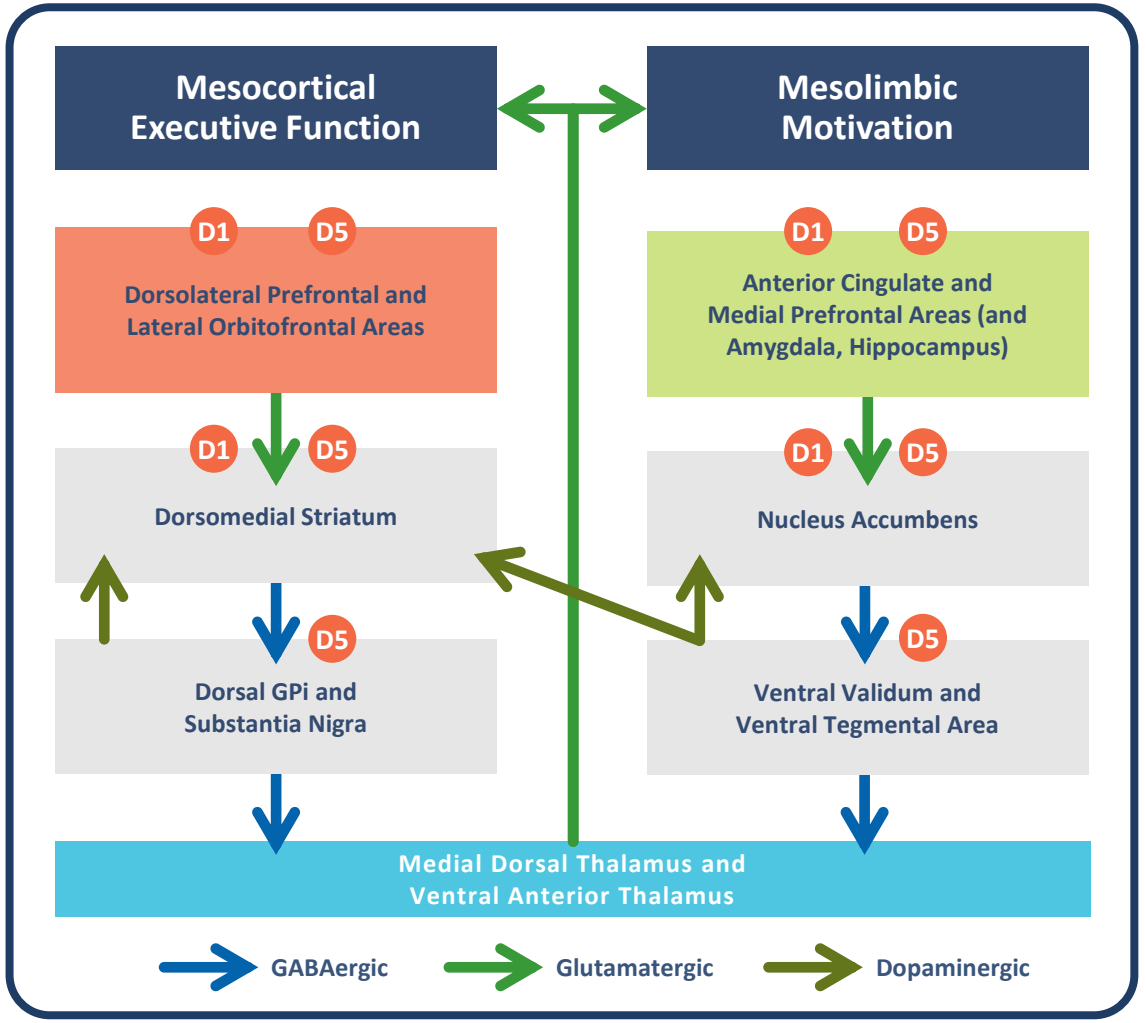


D1/D5 Pathway in Motivation and Reward

D1 CVL-871 is expected to enhance dopaminergic tone in key brain circuits

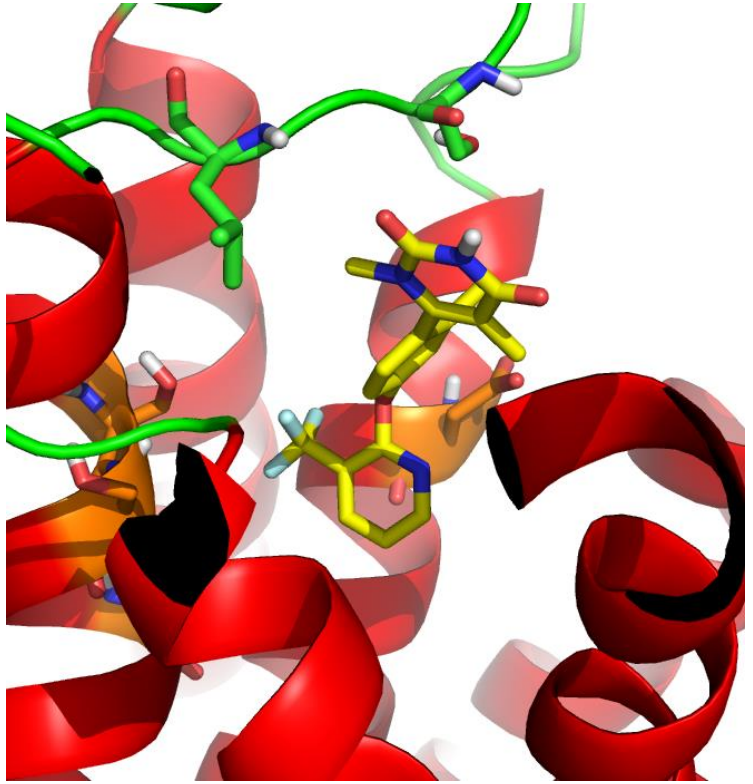


Conscious ***goal-directed behavior*** is mediated by the mesocorticolimbic dopamine circuit



CVL-871 – Receptor Pharmacology Profile

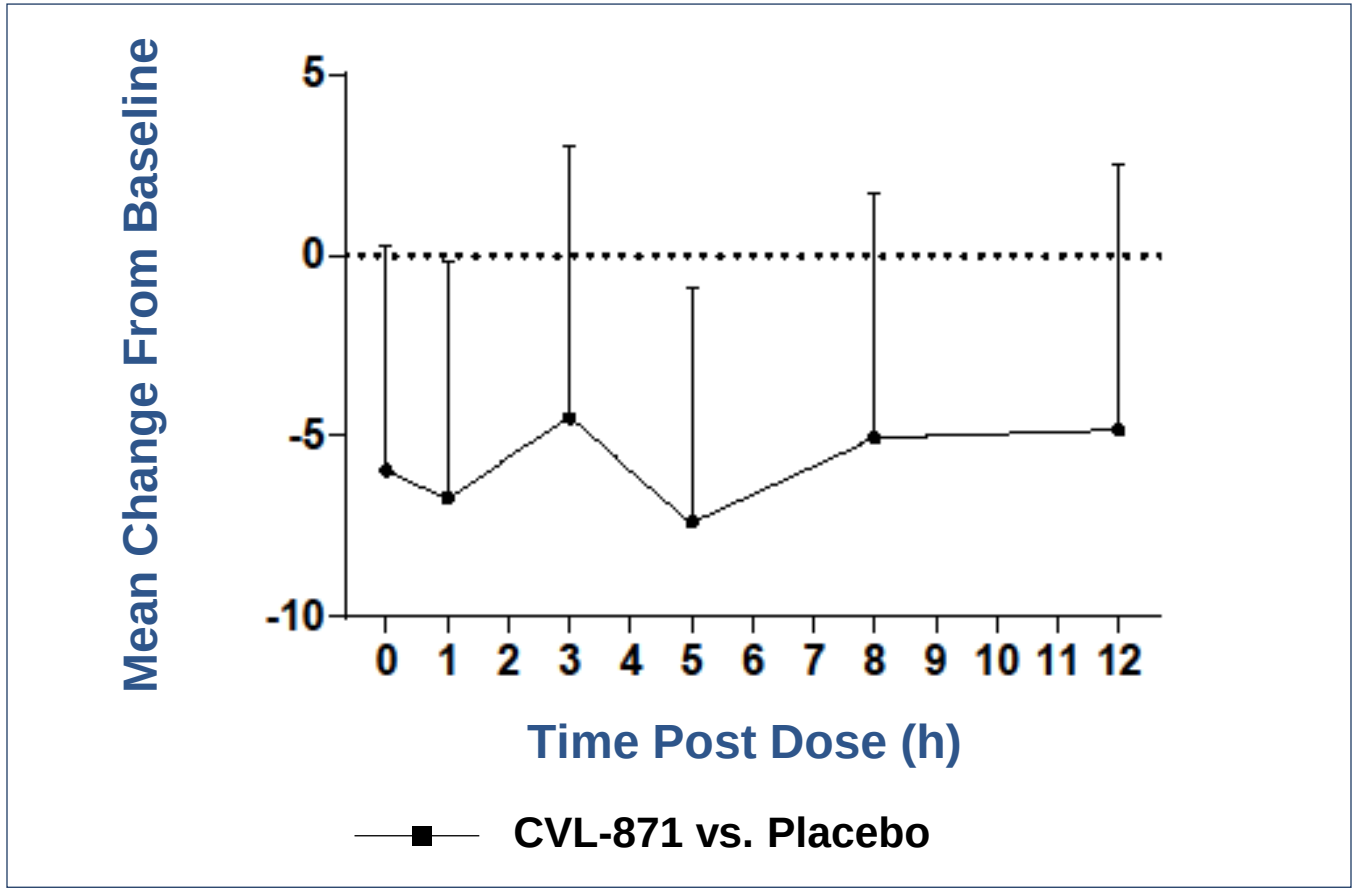
In vitro parameters	CVL-871
Agonism relative to dopamine	~40%
Selectivity vs D2/D3/D4 and >100 other targets	>250x
Human $T_{1/2}$	~24 hr



CVL-871 binds to D1 at dopamine site, but makes key novel contacts with the receptor

CVL-871 Demonstrated Target Engagement in Parkinson's Patients

MDS-UPDRS Part III Motor Function Scale



Proof of Pharmacology

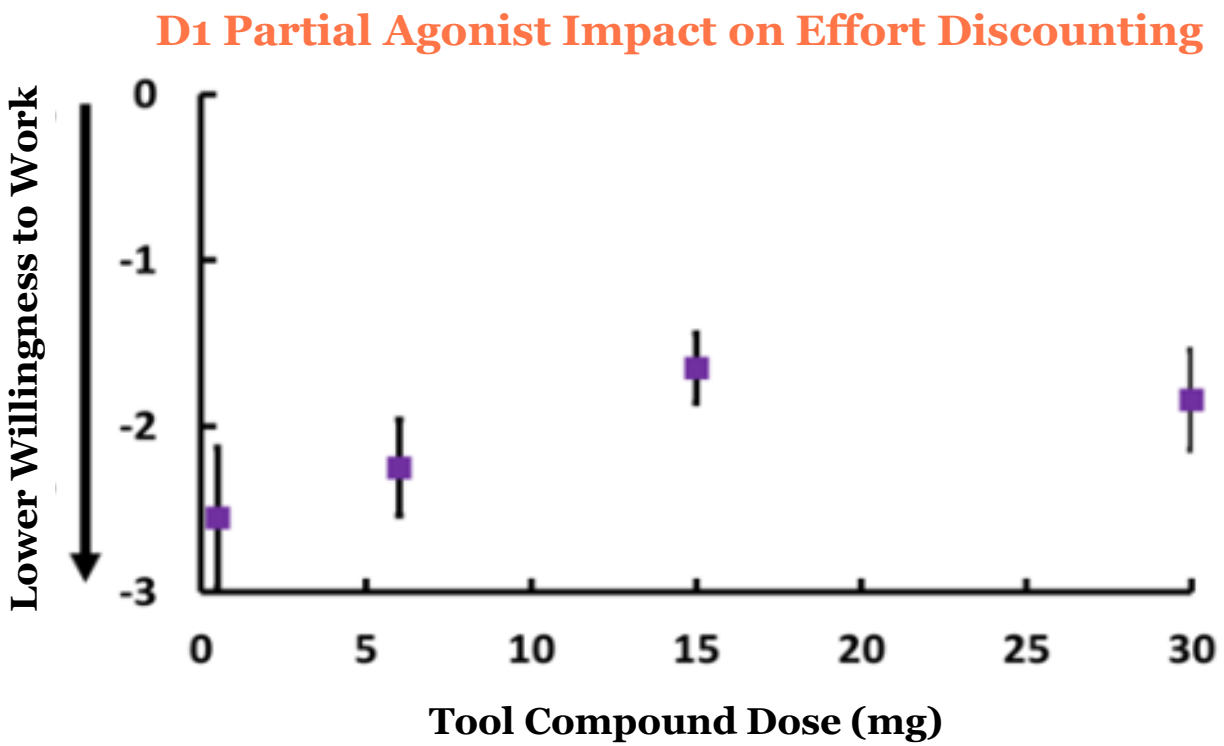
- CVL-871 modestly improved motor function (change from baseline) on day 7 of dosing in patients with moderate to advanced Parkinson's disease
- Data showed targeted modest dopamine partial agonist profile

Source: Clin Drug Investig. 2018 Jun;38(6):509-517.

Clinical Support for CVL-871 in Apathy

Clinical Translation of Neurocircuitry

D1/D5 partial agonist tool compound (similar profile to CVL-871) produced dose-related effects on effort and risk-based decision-making in healthy volunteers



Partial D1/D5 agonist increased willingness to work for better reward

Source: Biol. Psych. 2019 Apr; 87(7):678-685.

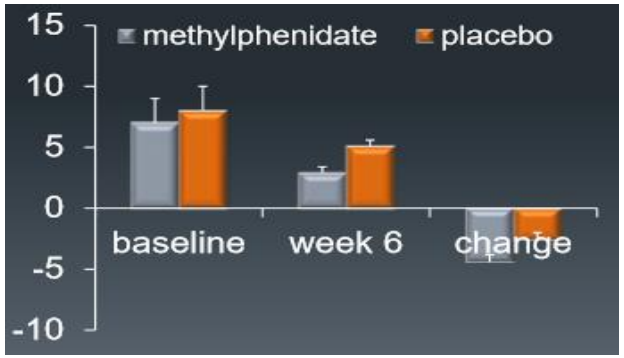
Increased D1/D5 Receptor Activation May Improve Apathy

D1/D5 Activation Potential in Apathy

- Dopamine acting via D1/D5 in the striatum directly promotes motivation and goal-directed behavior
- D1/D5 density reduces with age and reduction in dopamine signaling is associated with behavioral / psychological symptoms of dementia (BPSD)
- Methylphenidate (MPH), an NDRI*, significantly improved apathy in AD patients in 2 independent Phase 2 trials

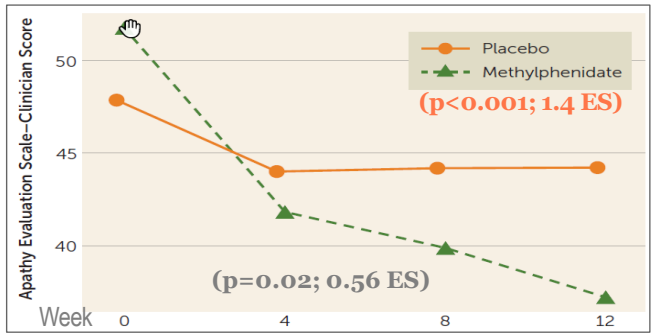
Methylphenidate Phase 2 Trials

ADMET1 Trial: showed NPI Apathy global score improvement of 1.8 points over placebo



ADMET1 Trial-Rosenberg, et al J Clin Psychiatry 2013

Veterans AD Apathy Trial: showed AES-C score improvement of 9.9 points over placebo at week 12



Veterans AD Apathy Trial, Padala et.al, Am J Psychiatry 2018

*NDRI = norepinephrine-dopamine reuptake inhibitor

Sources: Karrer etal, Neurobiol Aging 2017; Volkow etal, Am J Psychiatry, 1998; Flanigan et al, J. Neurosci., 2017

Phase 2a Trial in Dementia-Related Apathy

CVL-871 Phase 2a Exploratory Trial: Data Expected 2H 2022

Phase 2a Trial in Dementia-Related Apathy

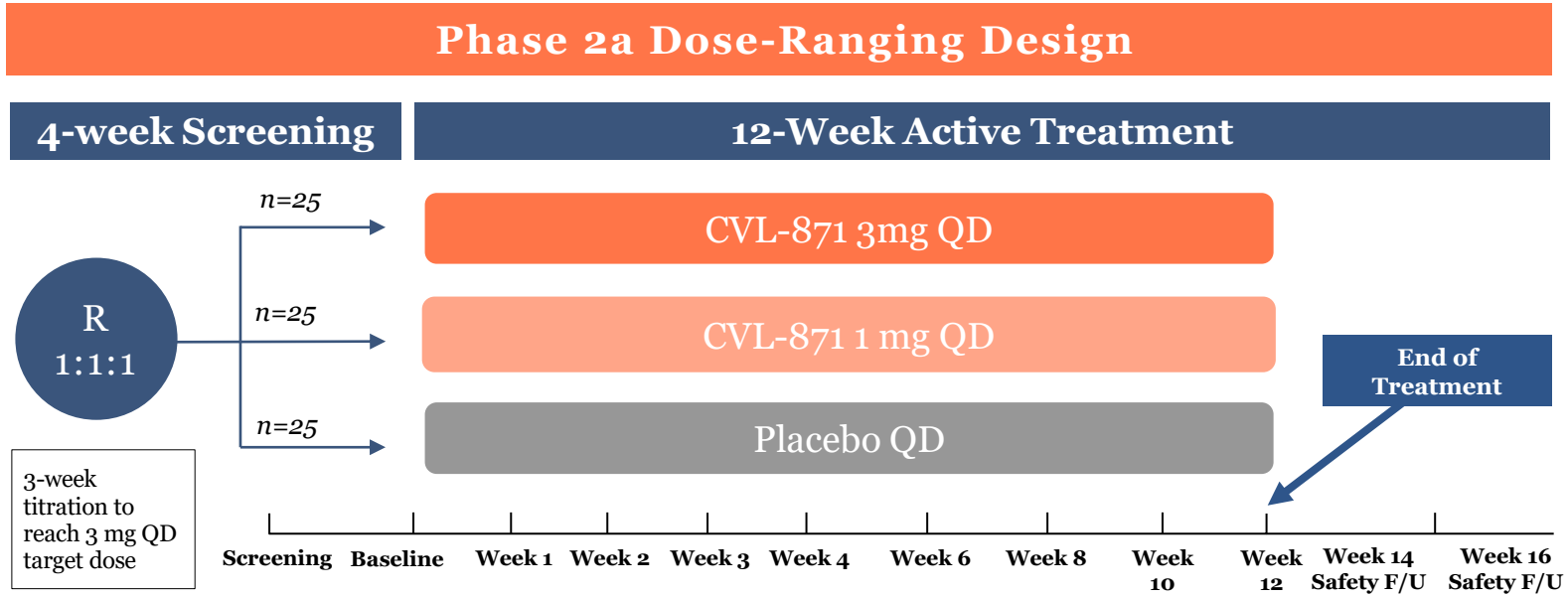
Key inclusion criteria

- Adults 50-85 years old
- NPI-Apathy domain frequency and severity scores each ≥ 2
- Mild-to-moderate dementia
- MMSE 15-26; CDR 0.5-2.0

No primary endpoint

Exploratory endpoints

- **Apathy/Global:** NPI/NPI-C, DAIR, AES-C, mADCS-CGIC/CGIS, Caregiver CGIC/CGIS
- **Function:** DAD, Zarit Caregiver Burden
- **Cognition:** ADAS-Cog13, Trail Making A, Digit Span, COWAT



Apathy Endpoints & Scale Validation

Example: NPI-C Apathy Domain

Responses should be based on the past 4 weeks.	Caregiver Interview			Patient Interview	Clinical Impression
	Frequency (0-4)	**Severity (0-3)**	**Distress (0-5)**	**Frequency (0-4)**	**Severity (0-3)**
1. Does subject seem less spontaneous and active than usual?					
2. Is subject less likely to initiate a conversation?					
3. Is subject less affectionate or lacking in emotions when compared to his/her usual self?					
4. Does subject contribute less to household chores?					
5. Does subject seem less interested in the activities and plans of others?					
6. Has subject lost interest in friends and family members?					
7. Is subject less enthusiastic about his/her usual interests?					
8. Does subject sit quietly without paying attention to things going on around him/her?					
9. Has subject reduced participation in social activities even when stimulated?					
10. Is subject less interested in or curious about routine or new events in his/her environment?					
11. Does subject express less emotion in response to positive or negative events?					

Total x/33

- NPI-C Apathy Domain is one of multiple established measures to evaluate apathy severity
- Conducting research to determine most appropriate fit-for-purpose measure to meet regulatory requirements
- The selected primary endpoint should accurately measure all aspects of disease as defined by the new diagnostic criteria that are important to clinicians, caregivers, and patients

Dementia-Related Apathy: A Clinical Perspective

Krista Lanctôt, Ph.D.*
Professor of Psychiatry & Pharmacology/Toxicology, University of Toronto

- Senior Neuroscientist and Head of Neuropsychopharmacology Research in Geriatric Psychiatry and in the Hurvitz Brain Sciences Program at Sunnybrook Research Institute
- Vice-Chair of Basic and Clinical Science in the Department of Psychiatry, Temerty Faculty of Medicine at the University of Toronto, Toronto
- Active researcher with over 300 publications
- Ph.D. in Clinical Pharmacology, University of Toronto

**Dr. Lanctot is an investigator in Cerevel's Phase 2a trial of CVL-871 in dementia-related apathy. She also sits on Cerevel's Clinical Advisory Board and is a paid consultant to Cerevel.*

Dementia-Related Apathy: A Clinical Perspective

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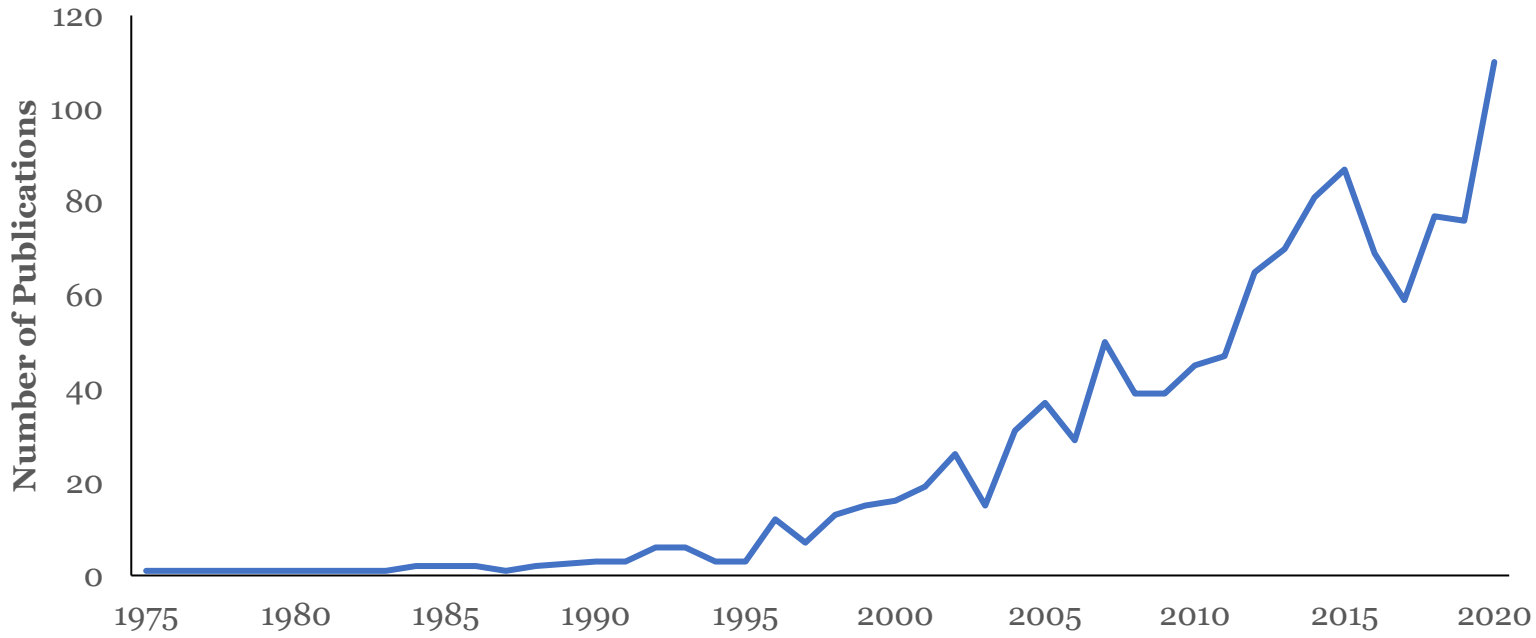
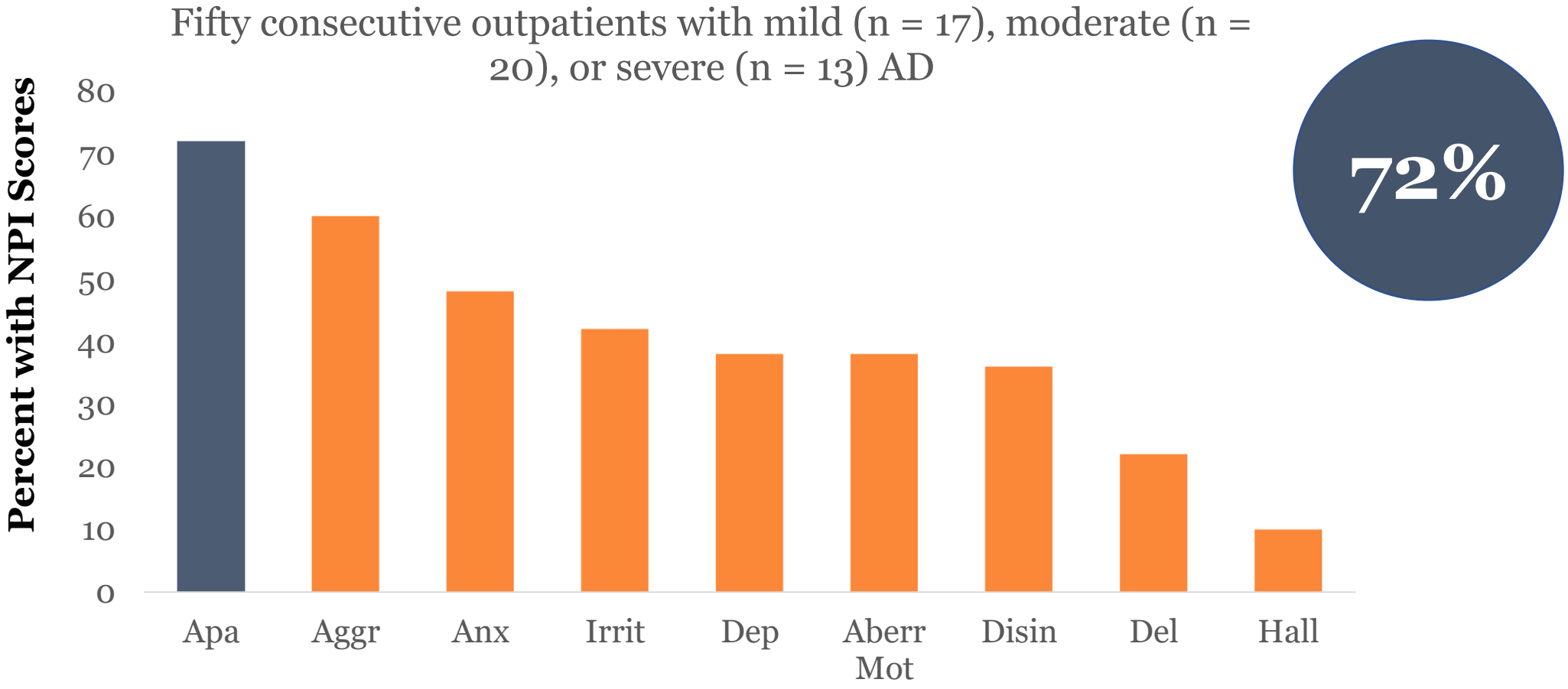
Apathy

- Increasing acknowledgement and interest in apathy in the medical and research communities



- Emerging focus for pharmacotherapy

Unmet Need: Apathy is the Most Common Neuropsychiatric Symptom in Alzheimer's Disease



Source: Mega et al, Neurology 1996; 46: 130-135

Unmet Need: Impact of Apathy on Patients and Care Partners

Apathy strongly correlated with caregiver burden

- 260 memory clinic outpatients with Alzheimer's disease [Chen et al 2017]

Which patient characteristics affected caregiver burden the most?

- 548 memory clinic outpatients
- Severity of cognitive impairment and apathy [Dauphinot et al 2015]

Sources: Dauphinot et al, J Alzheimer's Dis 2015; Chen et al, QJM Int J Med, 2017

What Does Apathy Look Like?
Diagnostic criteria in neurocognitive disorders

- Developed by International Society for CNS Clinical Trials and Methodology (ISCTM)
  - Input from academia, clinicians, and regulatory stakeholders

Received: 25 June 2020 | Revised: 26 March 2021 | Accepted: 5 April 2021

DOI: 10.1002/alz.12358

RESEARCH ARTICLE

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Diagnostic criteria for apathy in neurocognitive disorders

David S. Miller[1,#] | Philippe Robert[2,3,4,#] | Larry Ereshefsky[5] | Lawrence Adler[6] | Daniel Bateman[7] | Jeff Cummings[8,9] | Steven T. DeKosky[10] | Corinne E. Fischer[11,12] | Masud Husain[13,14,15] | Zahinoor Ismail[16] | Judith Jaeger[17] | Alan J. Lerner[18] | Abby Li[19] | Constantine G. Lyketsos[20] | Valeria Manera[2,3] | Jacobo Mintzer[21] | Hans J. Moebius[22] | Moyra Mortby[23] | Didier Meulien[24] | Stephane Pollentier[25] | Anton Porsteinsson[26] | Jill Rasmussen[27] | Paul B. Rosenberg[20] | Myuri T. Ruthirakuhan[19] | Mary Sano[28] | Carla Zucchero Sarracini[19] | Krista L. Lanctôt[19,29,#]

Sources: Miller et al, J Alzheimer's & Dementia 2021

The Patient with Apathy: A Triad of Symptoms

Sources: Miller et al, J Alzheimer's & Dementia 2021

Diminished Initiative

- Less spontaneous and/or active than usual self;
- Less likely to initiate usual activities
  - × Hobbies
  - × Chores
  - × Self-care
  - × Conversation
  - × Work-related or social activities

➢ **Impact: burden on care-partner**

➢ **Impact: patient quality of life**

Source: Miller et al, J Alzheimer's & Dementia 2021

Diminished Interest

- Less enthusiastic about usual activities
  - × Less interested in, or less curious about events in their environment
  - × Less interested in activities and plans made by others
  - × Less interested in friends and family
  - × Reduced participation in activities even when stimulated
  - × Less persistence in maintaining or completing tasks or activities

➢ **Impact: burden on care-partner**

➢ **Impact: patient quality of life**

Source: Miller et al, J Alzheimer's & Dementia 2021

Diminished Emotional Expression/Responsiveness

- Less spontaneous emotions
  - × Less affectionate compared to their usual self
  - × Expresses less emotion in response to positive or negative events
  - × Less concerned about the impact of their actions on other people
  - × Less empathy

➢**Impact: burden on care-partner**

➢**Impact: patient quality of life**

Caregivers often misinterpret apathy and find patients insensitive, ungrateful, uncaring

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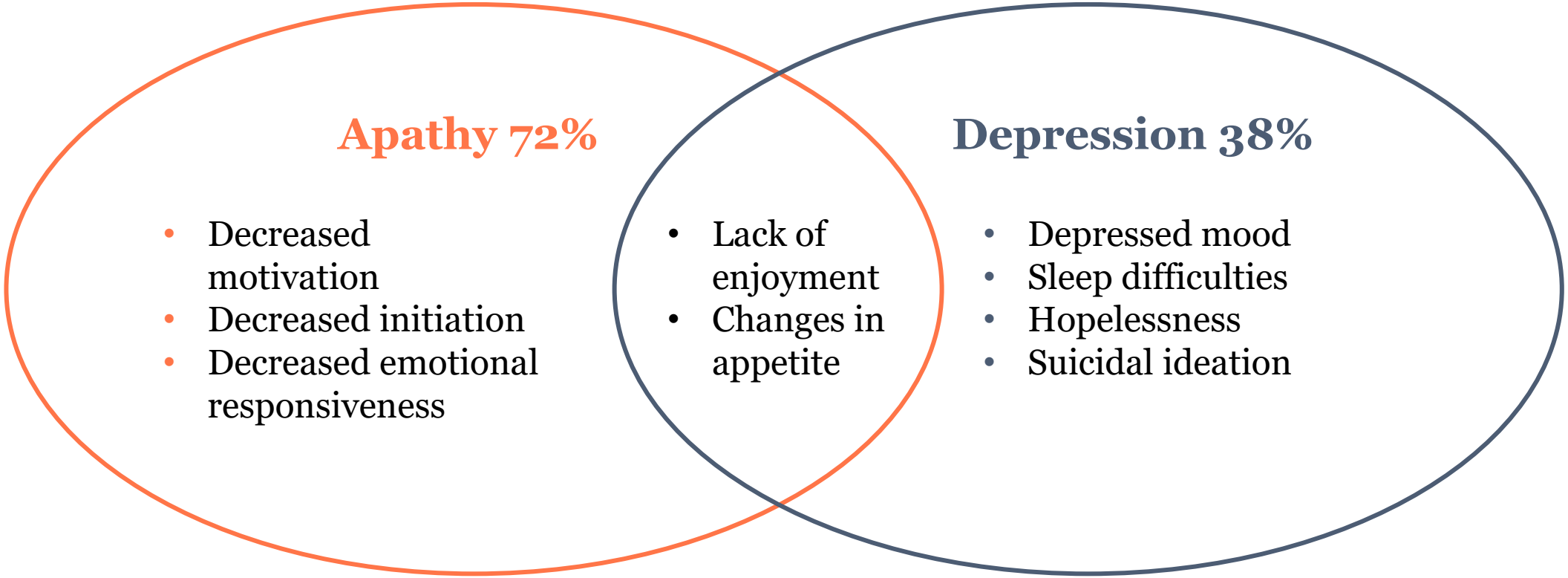
Source: Miller et al, J Alzheimer's & Dementia 2021

Apathy vs. Depression: Similarities and Differences



- Apathy is characterized by a lack of affect while depression is characterized by the overwhelming presence of a negative affect and mood.

Apathy vs. Depression – Clearly Distinguished on the NPI

E. Dysphoria

Does (S) seem sad or depressed? Does (S) say that he/she feels sad or depressed?

Responses should be based on the past 4 weeks.

Description
1. Does (S) have periods of tearfulness or sobbing that seem to indicate sadness?
2. Does (S) say he/she is sad or in low spirits or acts as if he/she is sad or in low spirits?
3. Does (S) put him/herself down or say that he/she feels like a failure?
4. Does (S) seem very discouraged or say he/she has no future?
5. Does (S) say he/she is a burden to the family and that the family would be better off without him/her?
6. Does (S) express a wish for death or talk about killing him/herself?
7. Does (S) say that he/she is a bad person and deserves to be punished?
If you are also completing the original NPI, please ask the informant to provide the following global domain ratings for shaded items only: Frequency (0-4) _____ Severity (0-3): _____ Caregiver Distress (0-5): _____ Frequency x Severity: _____
8. Does (S) have a worried or pained expression?
9. Is (S) pessimistic or overly negative, expecting the worst?
10. Is (S) suddenly irritable or easily annoyed?
11. Has (S) changed in his/her eating habits, such as eating more/less or more/less often than usual?
12. Does (S) talk about feeling guilty for things that for which he/she had no control over?
13. Does (S) seem to no longer enjoy previously enjoyable activities?

H. Apathy/Indifference

Has (S) lost interest in the world around him/her? Has (S) lost interest in doing things or lack motivation for starting new activities? Is (S) more difficult to engage in conversation or in doing chores? Is (S) apathetic or indifferent?

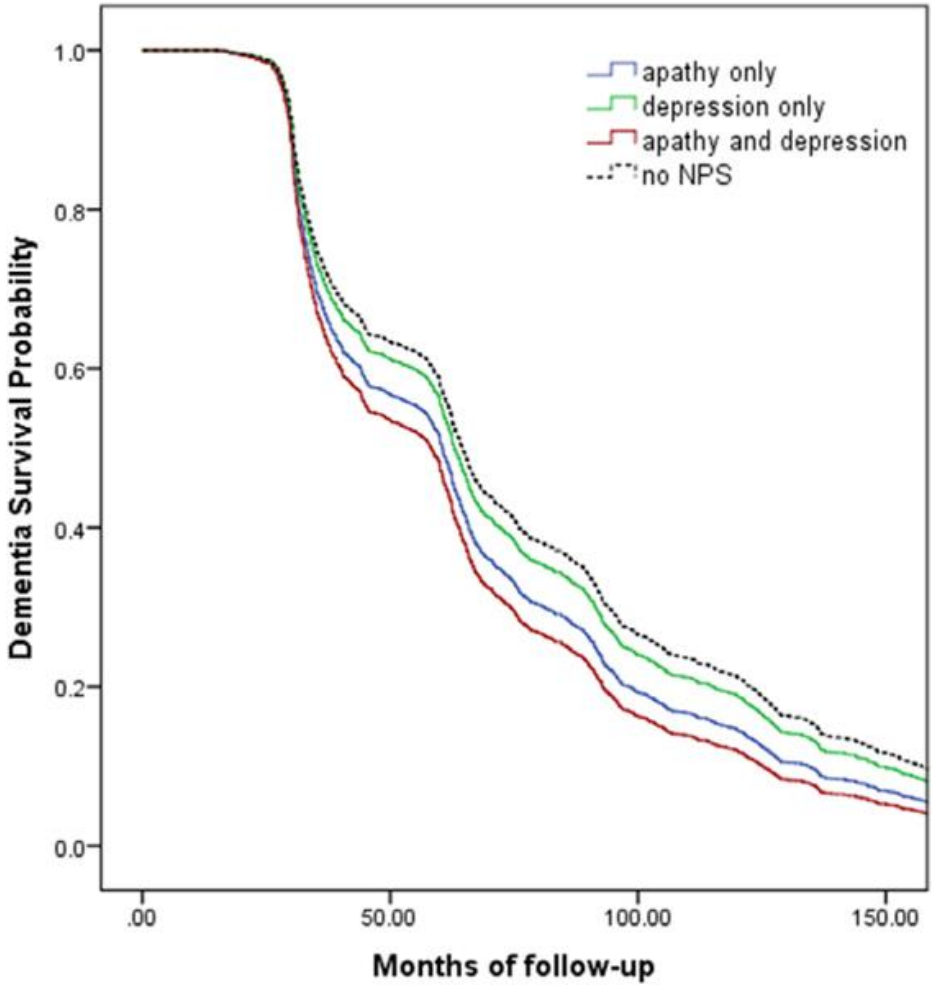
Responses should be based on the past 4 weeks.

Description
1. Does (S) seem less spontaneous and active than usual?
2. Is (S) less likely to initiate a conversation?
3. Is (S) less affectionate or lacking in emotions when compared to his/her usual self?
4. Does (S) contribute less to household chores?
5. Does (S) seem less spontaneous and active than usual?
6. Does (S) seem less interested in the activities and plans of others?
7. Has (S) lost interest in friends and family members?
8. Is (S) less enthusiastic about his/her usual interests?
9. Does (S) sit quietly without paying attention to things going on around him/her?
If you are also completing the original NPI, please ask the informant to provide the following global domain ratings for shaded items only: Frequency (0-4) _____ Severity (0-3): _____ Caregiver Distress (0-5): _____ Frequency x Severity: _____
10. Has (S) reduced participation in social activities even when stimulated?
11. Is (S) less interested in or curious about routine or new events in his/her environment?
12. Does (S) express less emotion in response to positive or negative or events?

Apathy, but Not Depression, Predicts Increased Risk of AD

- Compared with those without NPS
  - 686 apathy + depression, 40% increase
  - 388 were apathy-only, 20% increase
  - 1514 depression-only, no increase in risk of conversion to AD

- n=4932 MCI, median follow-up 1.9 years, 1713 (34.7%) converted to AD



Source: Ruthirakuhan et al, Am J Geriatr Psychiatry. 2019

What Does "Improved Apathy" Look Like?

Apathy in Dementia Methylphenidate Trial (ADMET) And ADMET 2

FOCUS ON ALZHEIMER'S DISEASE AND RELATED DISORDERS

Safety and Efficacy of Methylphenidate for Apathy in Alzheimer's Disease: A Randomized, Placebo-Controlled Trial

Paul B. Rosenberg, MD; Krista L. Lanctôt, PhD; Lea T. Drye, PhD; Nathan Herrmann, MD; Roberta W. Scherer, PhD; David L. Bachman, MD; and Jacobo E. Mintzer, MD, MBA, for the ADMET investigators

JAMA Neurology | Original Investigation

Effect of Methylphenidate on Apathy in Patients With Alzheimer Disease
The ADMET 2 Randomized Clinical Trial

Jacobo Mintzer, MD, MBA; Krista L. Lanctôt, PhD; Roberta W. Scherer, PhD; Paul B. Rosenberg, MD; Nathan Herrmann, MD; Christopher H. van Dyck, MD; Prasad R. Padala, MD; Olga Brawman-Mintzer, MD; Anton P. Porsteinsson, MD; Alan J. Lerner, MD; Suzanne Craft, PhD; Allan I. Levey, MD, PhD; William Burke, MD; Jamie Perin, PhD; David Shade, JD; for the ADMET 2 Research Group

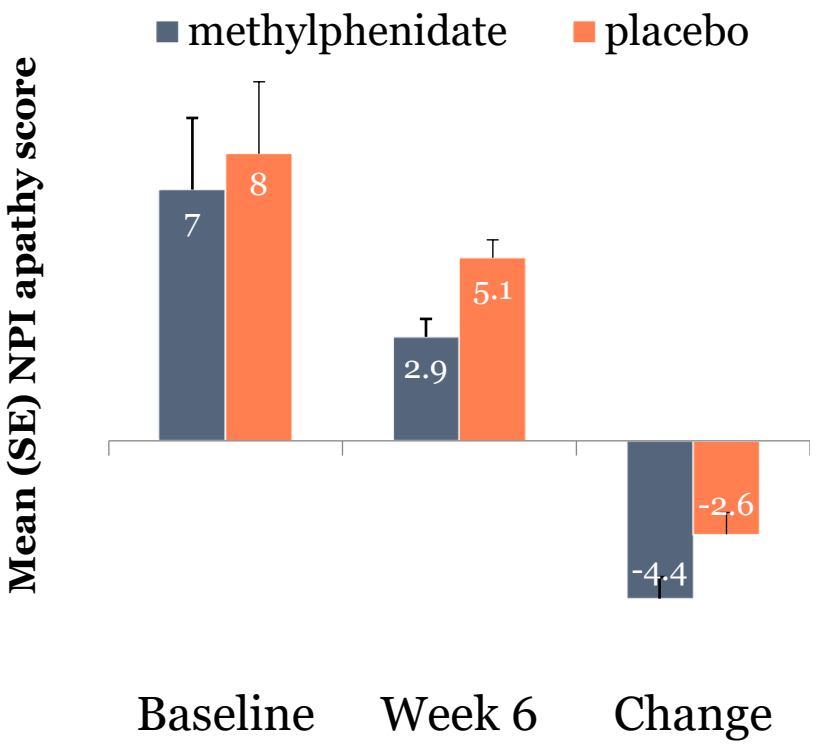
Longer duration Meds + Psychosocial

Sources: Rosenberg et al J Clin Psychiatry 2013; Mintzer el al, JAMA Neurology 2021

What Does "Improved Apathy" Look Like?

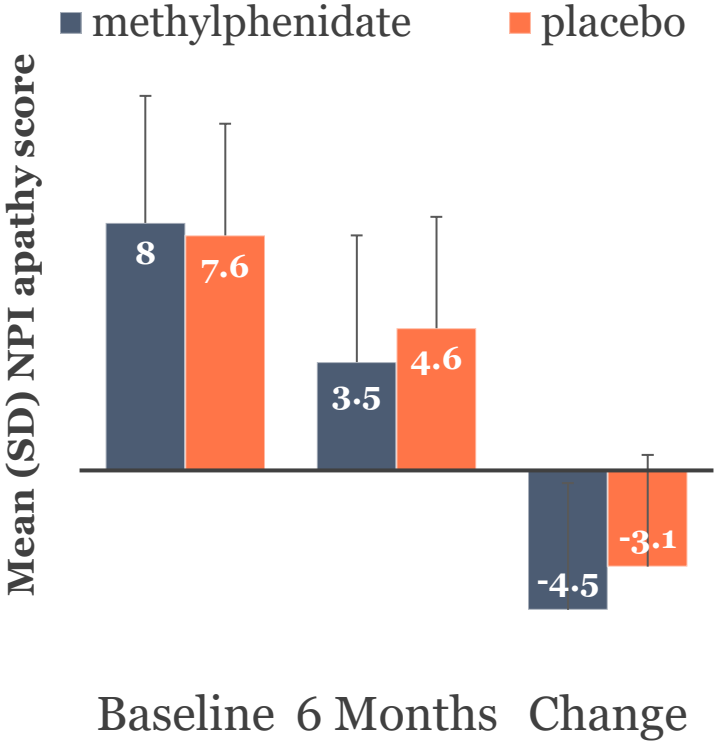
✓ Caregivers report fewer apathy symptoms

ADMET Results



NPI apathy score improvement 1.8 points (95% CI 0.3, 3.4) greater in methylphenidate vs. placebo (p=0.02)

ADMET 2 Results



NPI apathy score improvement 1.3 points (95% CI 0.5, 2.0) greater in methylphenidate vs. placebo (p=0.002)

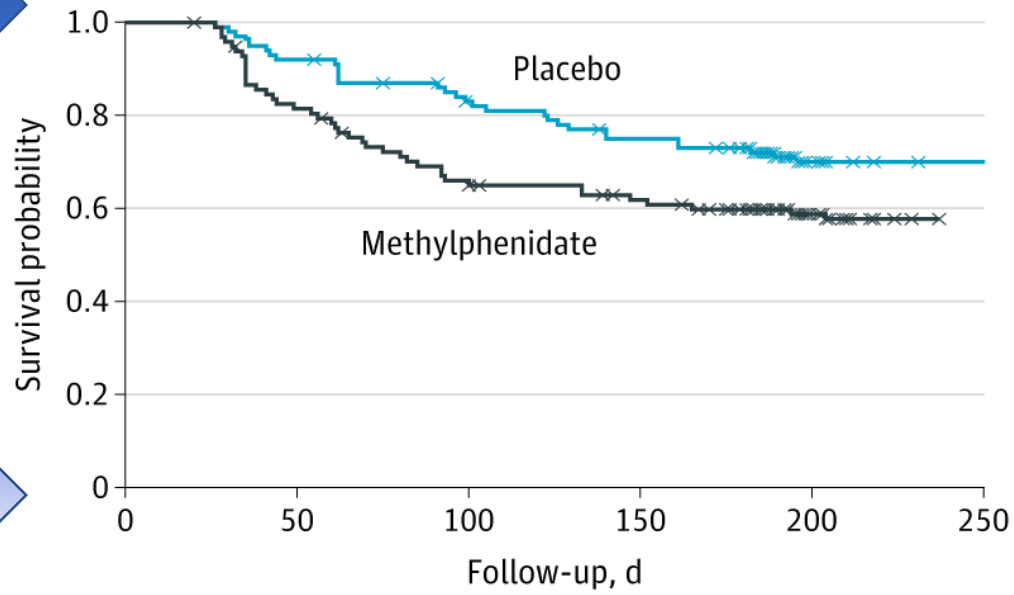
Sources: Rosenberg et al J Clin Psychiatry. 2013; Mintzer el al, JAMA Neurology 2021

What Does "Improved Apathy" Look Like?

✓ More people with no apathy

Proportion of patients achieving an apathy score of zero

apathy



No apathy

No. at risk						
Methylphenidate	97	78	61	53	14	0
Placebo	100	91	78	69	8	1

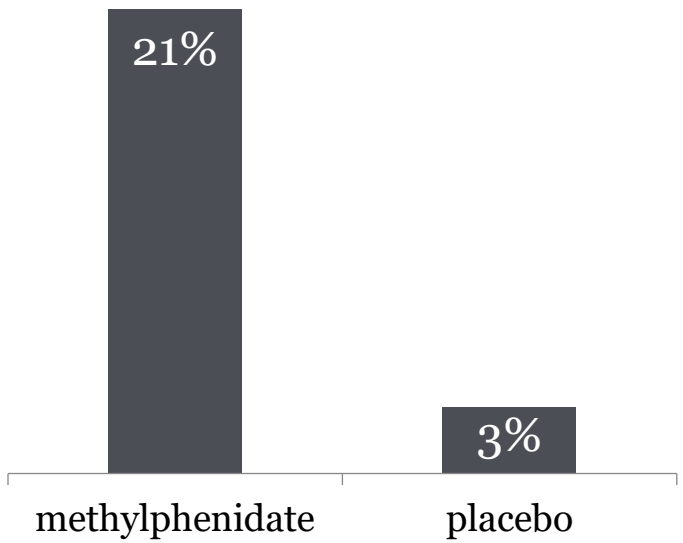
- At month 6, 27% (24 of 89) of participants in the methylphenidate group had an NPI apathy score of 0 compared with 14% (13 of 90) in the placebo group

Source: Mintzer el al, JAMA Neurology 2021

What Does "Improved Apathy" Look Like?
✓ More patients rated as improved clinically by the physician

Results from ADMET

% moderate or marked improvement on CGI-C

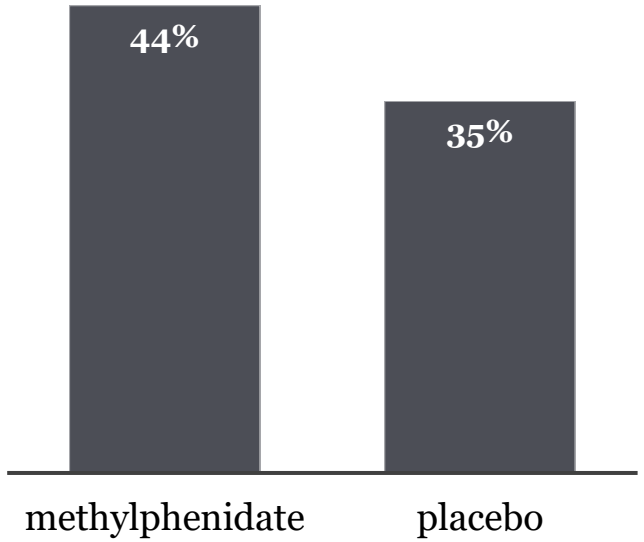


Odds ratio (95% CI) for improvement in CGI-C was 3.7 (1.3, 10.8) (p=0.02)

Clinically meaningful

Results from ADMET 2

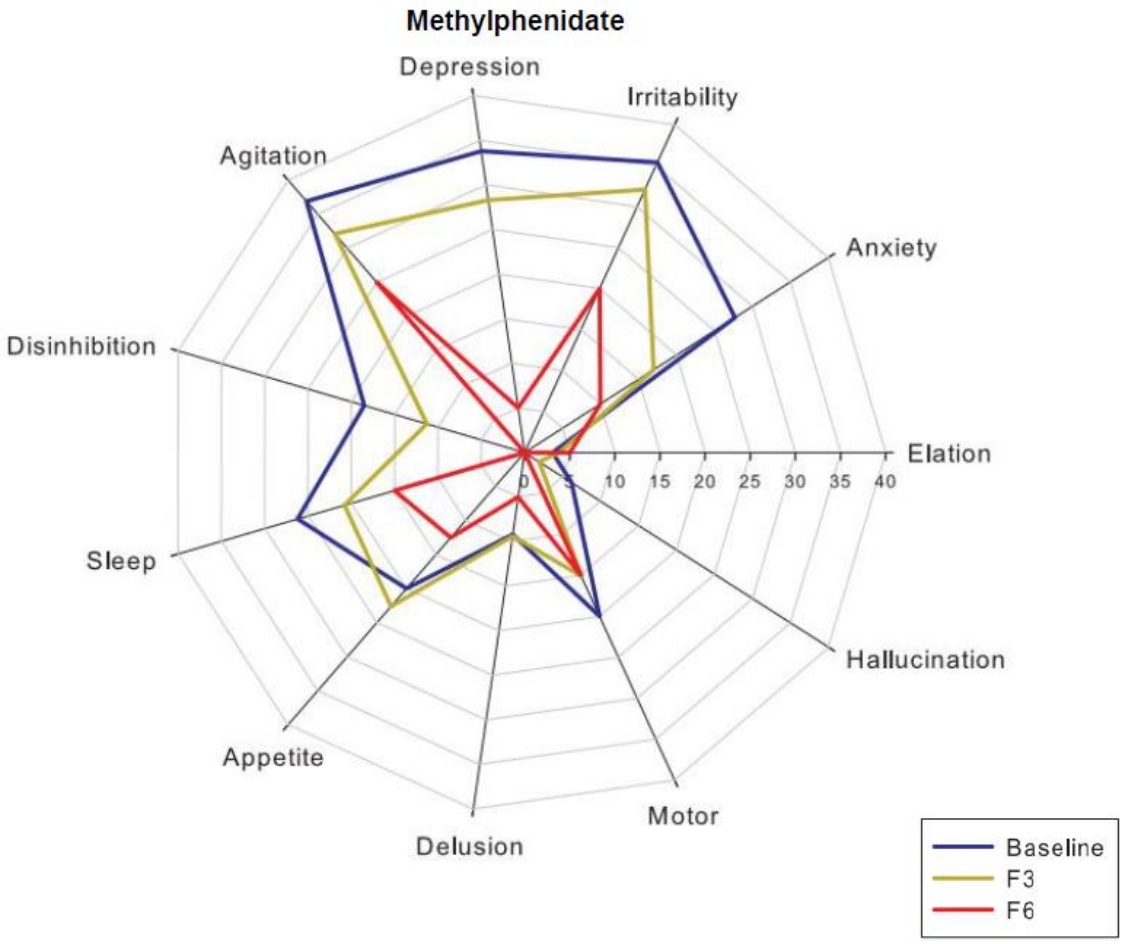
% improved over 6 months



Estimated difference in average change from baseline to 6 months (methylphenidate versus placebo), OR (95% CI) 1.43 (1.00, 2.04); P = 0.048

Sources: Rosenberg et al J Clin Psychiatry.2013; Mintzer el al, JAMA Neurology 2021

What Does Improved Apathy Look Like?
✓ Selective for apathy (ADMET 2)



- No change in other neuropsychiatric symptoms, except for increased NPI aberrant motor behavior in the methylphenidate compared with the placebo group (mean difference 0.69; 95% CI, 0.09-1.25; $P = .03$)

Source: Mintzer el al JAMA Neurology 2021

What Does "Improved Apathy" Look Like?
✓ Improvements in other symptoms reported

- Short-term:
  - Improvement in cognition, improved functional status, decreased caregiver burden (Padala et al 2016)
  - Improvement in cognition in ADMET (Rosenberg et al 2013, Lanctot et al 2014)

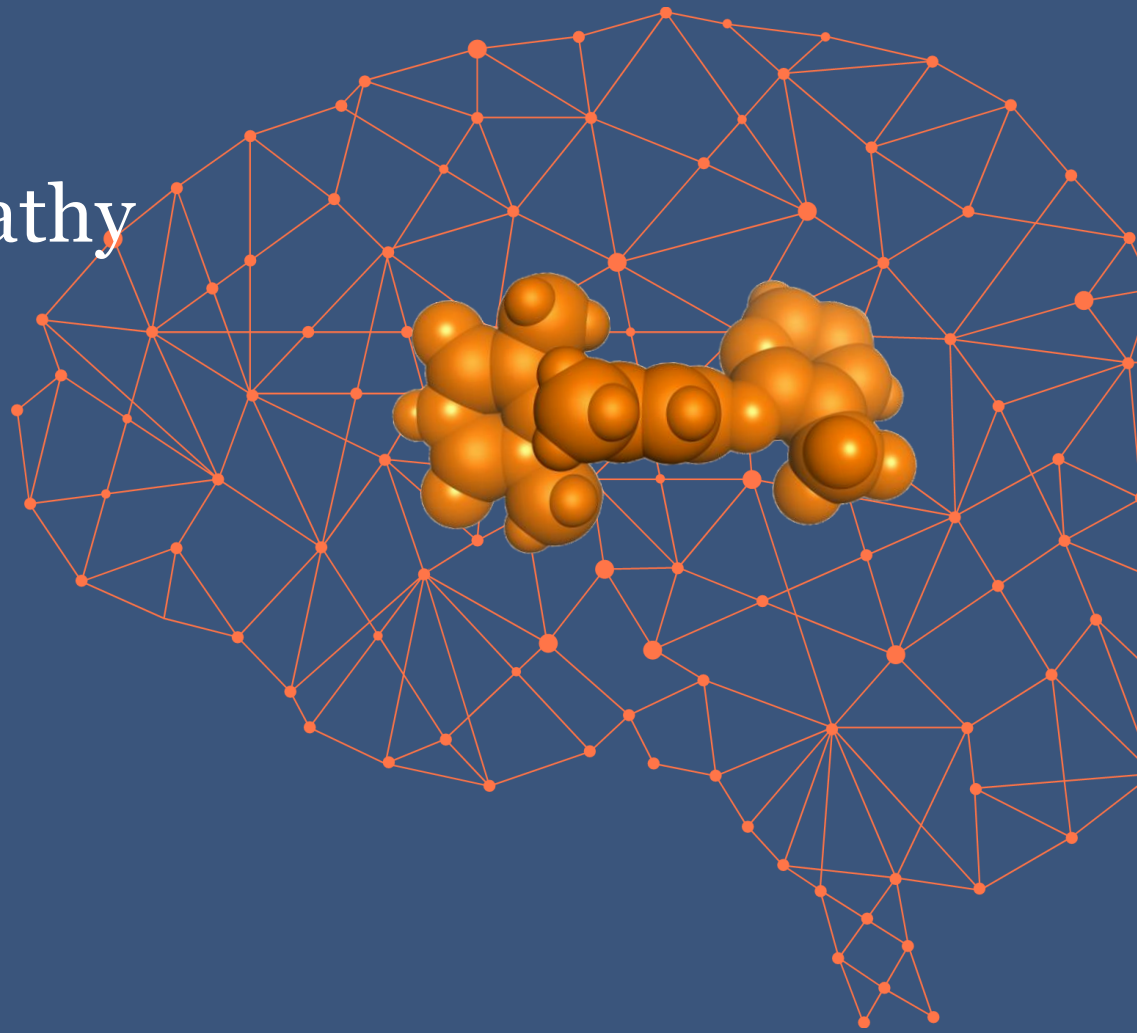
- Longer term:
  - Improvement in apathy correlated with overall clinical improvement and decreased caregiver burden in ADMET2 (Mintzer et al 2021)

cerevel

Sources: Padala et al Am J Psychiatry 2016, Rosenberg et al J Clin Psychiatry 2013, Lanctôt et al Int Psychogeriatr. 2014, Mintzer el al JAMA Neurology 2021

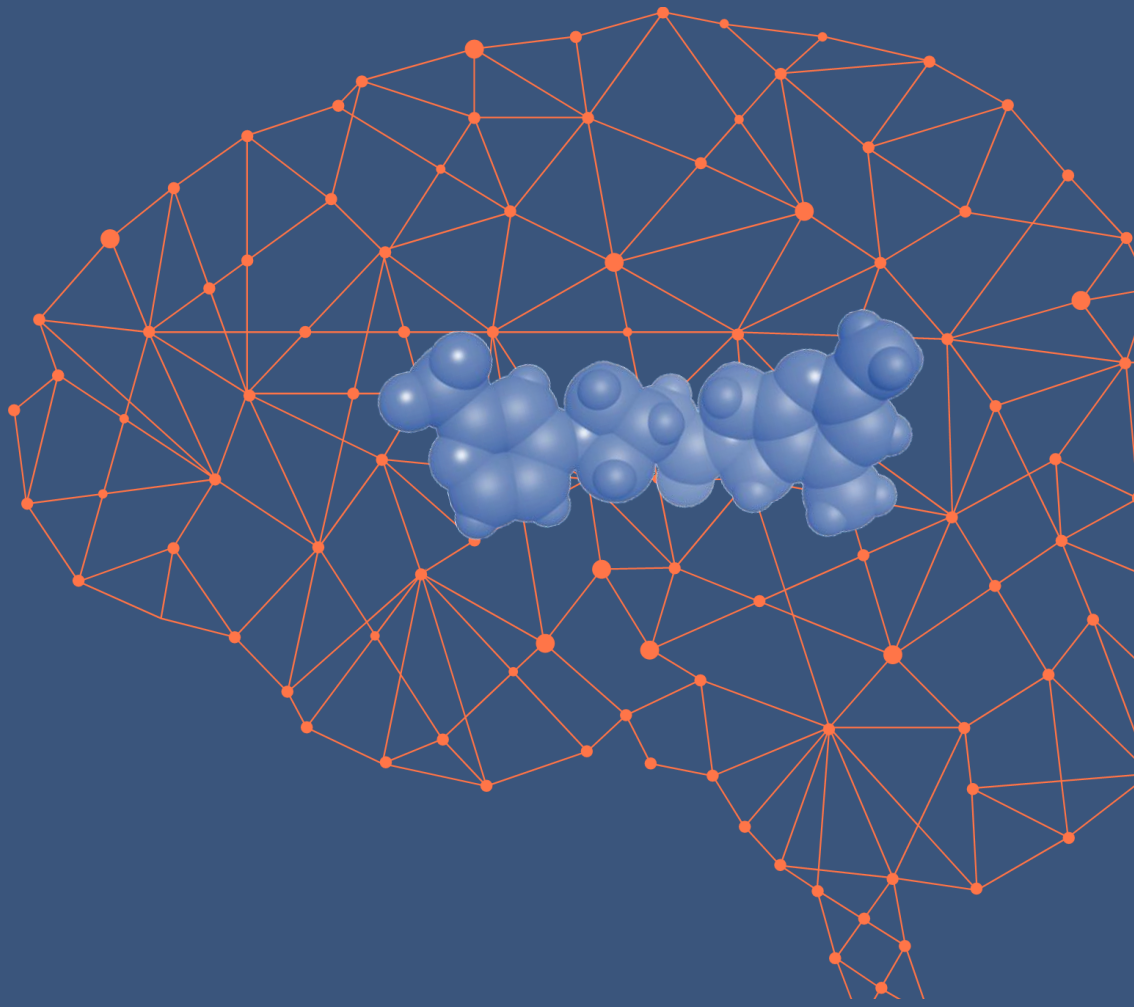
CVL-871 in Dementia-Related Apathy

Partial agonist selectively targeting the dopamine D1 receptor with the goal of modulating motivation and reward pathways to address apathy in patients with mild-to-moderate dementia



CVL-231 in Schizophrenia

Selectively targeting the M4 muscarinic receptor with the goal of treating psychosis-related symptoms with improved side effect profile



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Cerevel's M4 PAM is a Potential Next Generation Antipsychotic

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

First-in-Class Therapy with Novel MOA

M4 Selective

Targeted Muscarinic Activity

Improved Tolerability

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

Large Market

- ~20M Patients Worldwide
- ~$7B G7 Revenues in 2018
- ~3.5% Growth per year

Significant Need for New Treatment Option

- Side Effect and Tolerability Issues
  - *Lead to* → Limited Compliance (60%)
    - → High Relapse Rates (77% at 1 year; 90% at 2 years)
      - *Lead to* → Progression and worsening of disease
        - *Lead to* → Side Effect and Tolerability Issues
- High Discontinuation (74%) Within 18 months

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

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

Receptor Selectivity Offers Potential Improvement over Non-Selective Compounds

Xanomeline (M1/M4 agonist) data showed targeting muscarinic receptor may improve psychosis

But development limited by GI and CV side effects

Karuna's KarXT addresses tolerability issues by adding trospium to xanomeline to offset side effects

Combination approach with non-selective peripheral antagonist

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

M1 receptors believed to contribute to GI side effects, potential cognitive benefit undetermined

CVL-231's Differentiated Approach

Target	• Highly selective for M4 receptor
Antipsychotic effect	• 19.5 pt improvement in PANSS total score at Week 6
Tolerability	• No GI-related dropouts • Not associated with EPS, akathisia, or weight gain
Dosing	• Once-daily
Titration	• None

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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EPS = Extrapyramidal symptoms

CVL-231 Speaker Bios

Matthew Leoni, M.D., M.B.A.
Vice President, Global Clinical Development

- Joined Cerevel March 2019
- 13 years of clinical development experience at Galderma, Novartis & Otsuka
- M.D. from University of Pennsylvania, M.B.A. from Drexel University

Sridhar Duvvuri, Ph.D.
Vice President, Clinical Pharmacology and Pharmacometrics

- Joined Cerevel May 2019
- 13 years at Pfizer
- Expertise in early clinical development, pharmacokinetics, pharmacodynamics and PK/PD modeling
- Ph.D. in Pharmacokinetics & Drug Delivery from University of Missouri—Kansas City

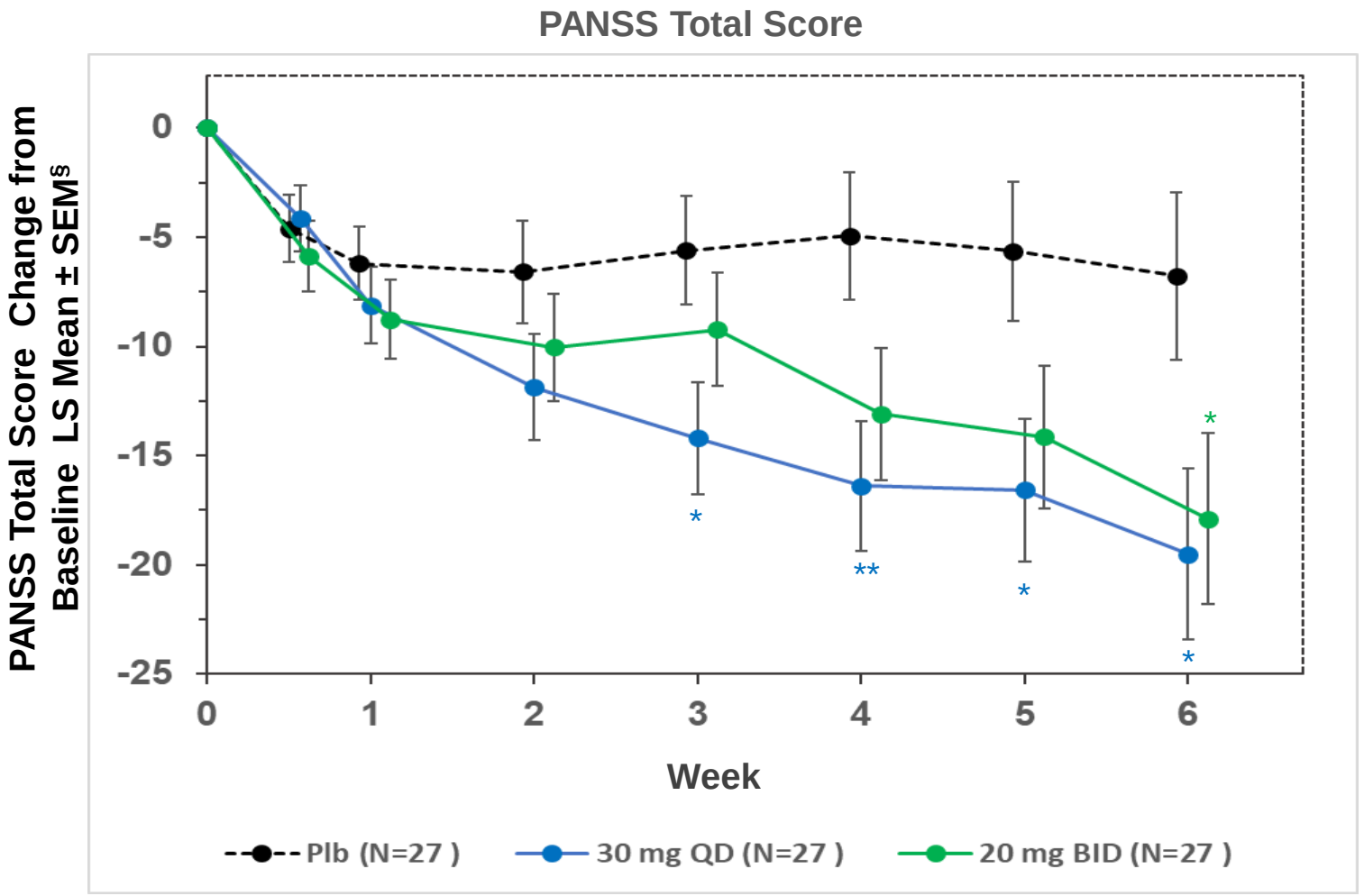
Phase 1b Topline Results

Phase 1b in Schizophrenia: Topline Results

- **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, akathisia, or weight gain
  - Gastrointestinal (GI) side effects were infrequent and were similar between treatment and placebo
  - Serious adverse events included COVID-19, accidental overdose (cocaine), and exacerbation of schizophrenia (one instance of each); none considered related to study medication

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

Phase 1b: 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.

Phase 1b: 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%)

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%)

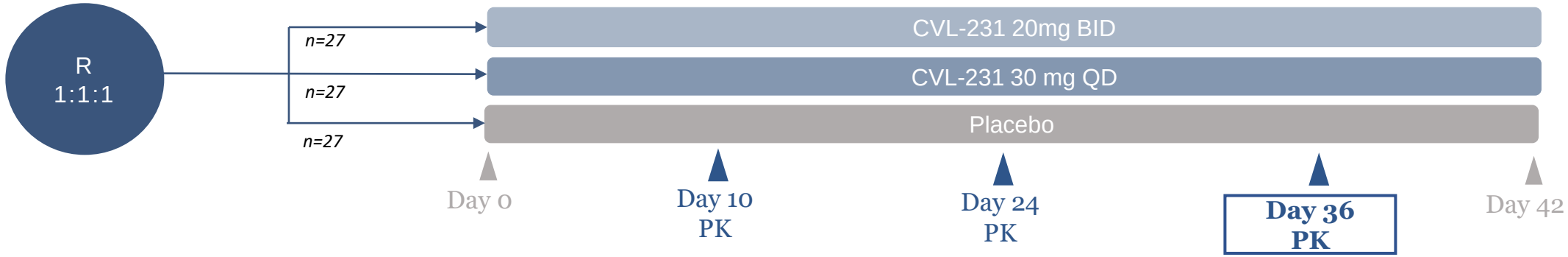
***AEs leading to discontinuation of treatment with IMP. No other AE leading to discontinuation of IMP*

* 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.

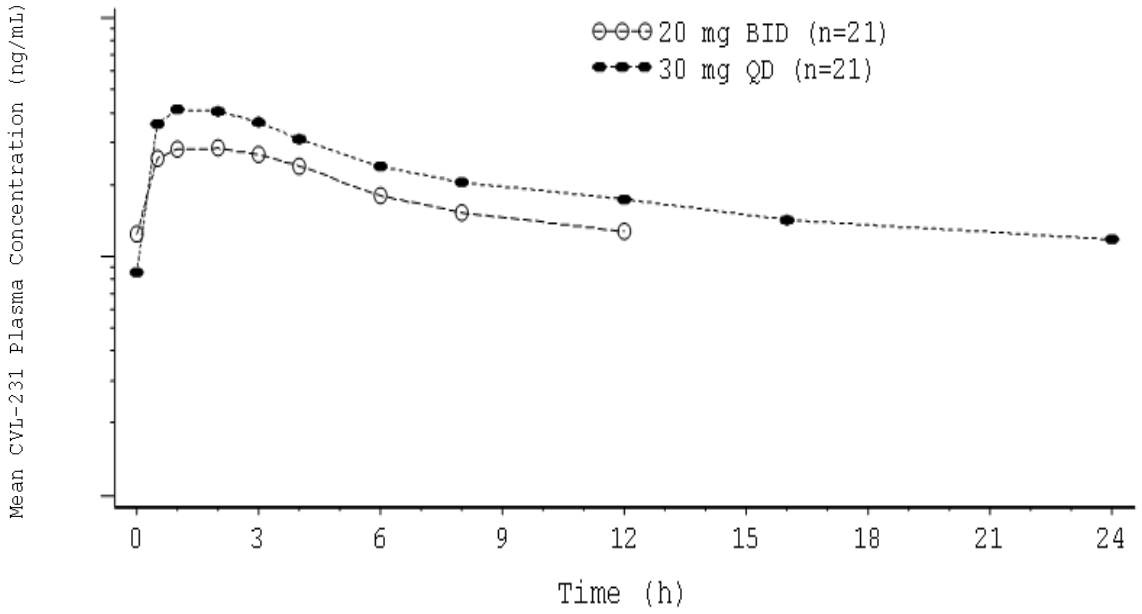
PK & Receptor Occupancy Data

Phase 1b PK Data Suggests Once-Daily Dosing for Future Studies

Phase 1b Part B Design: PK Assessment on Day 36*



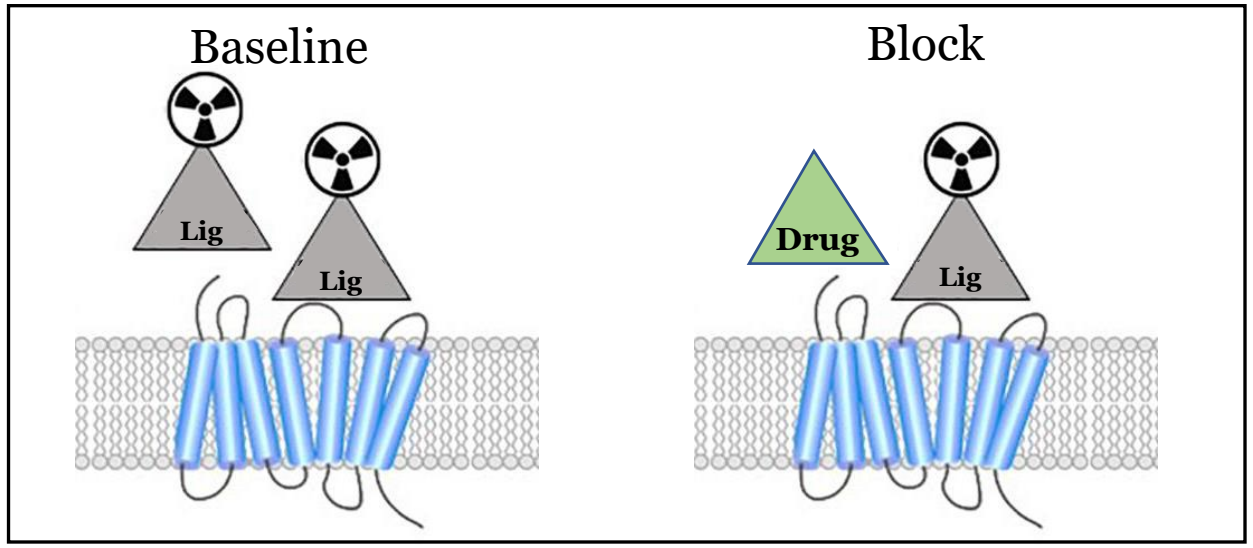
CVL-231 Plasma Concentration-time Profile (Day 36)

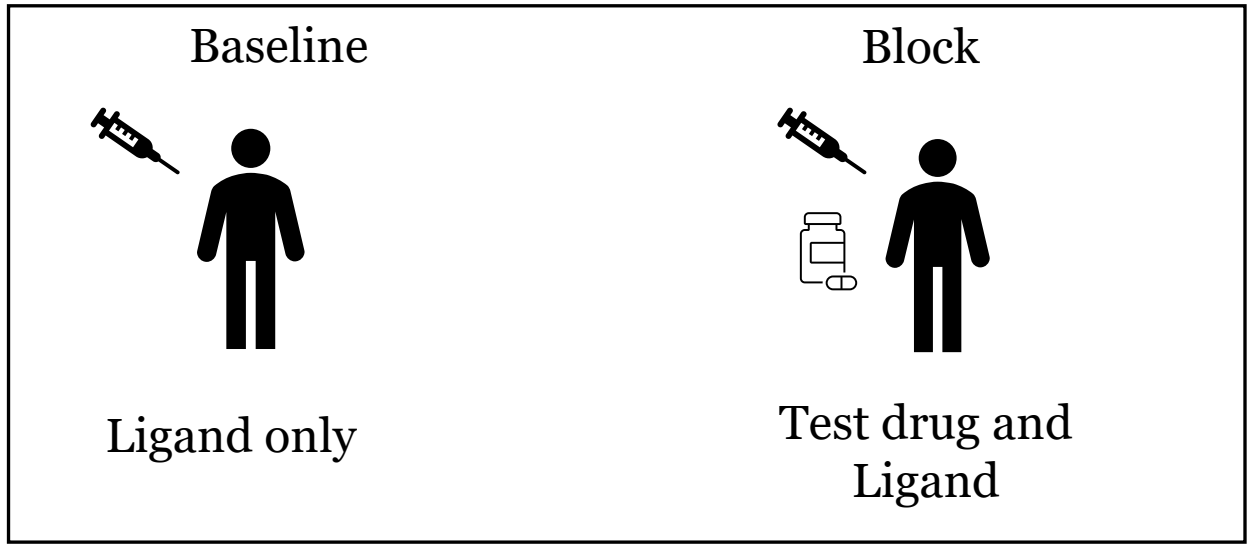


- Both doses in Phase 1b trial resulted in similar exposure levels through course of the day
- Review of antipsychotic results combined with PK data suggest once-daily dosing is most appropriate for evaluation in future trials

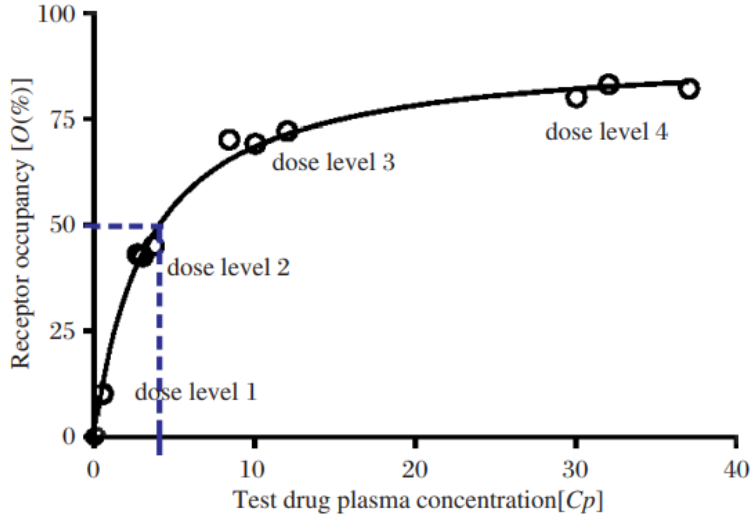
*PK samples were obtained pre-dose and at 0.5, 1, 2, 3, 4, 6, 8, 12, 16, and 24 hours following administration of the morning dose on Day 36. PK samples were only taken pre-dose and at 1, 4, and 8 hours following the morning dose on Days 10 and 24.

PET RO Studies for Understanding Target Engagement



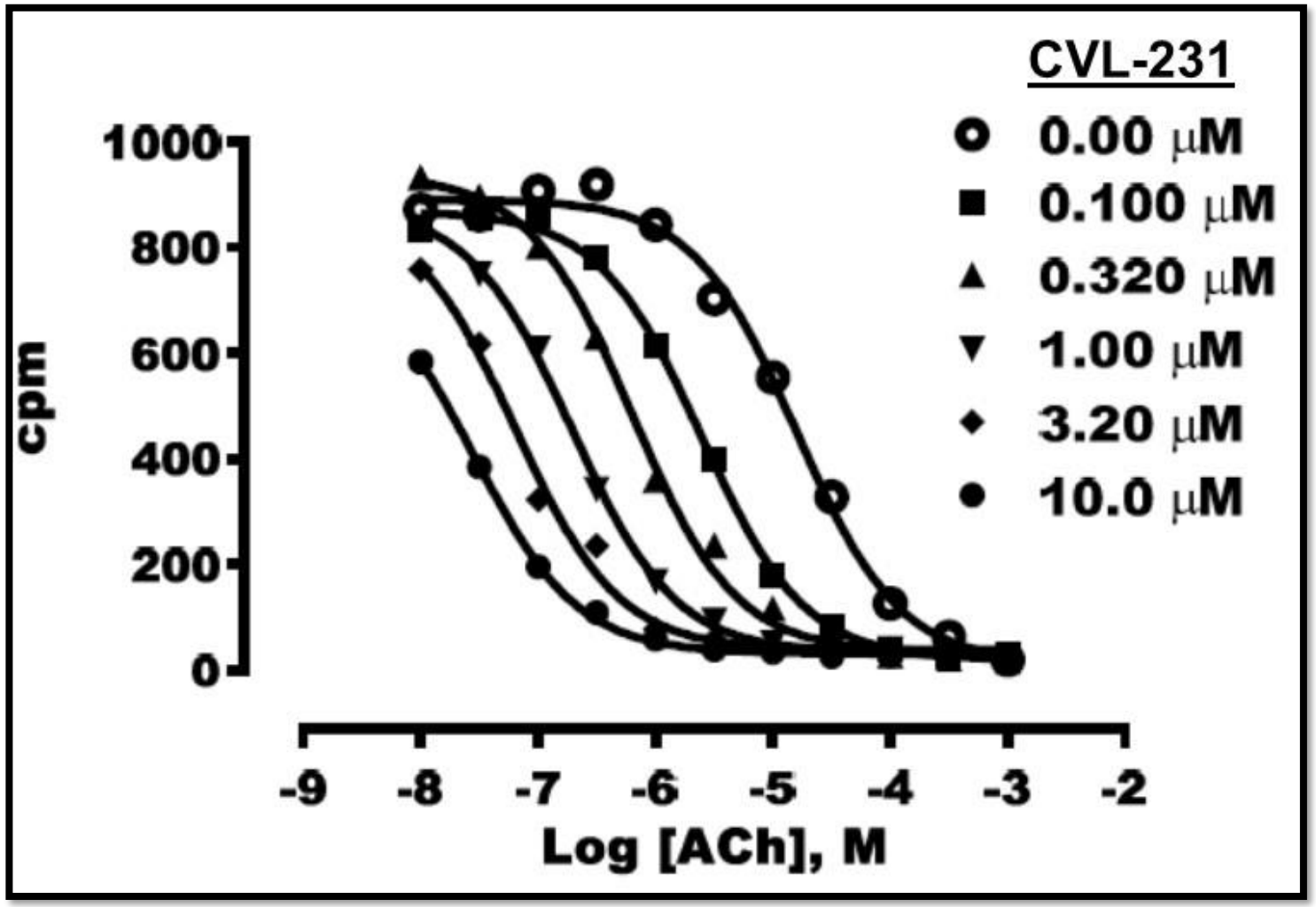


- PET RO studies are designed to understand the target occupancy of test drugs at their target sites
- Studies involve administration of a tracer to understand target binding followed by displacement of the tracer by test drugs



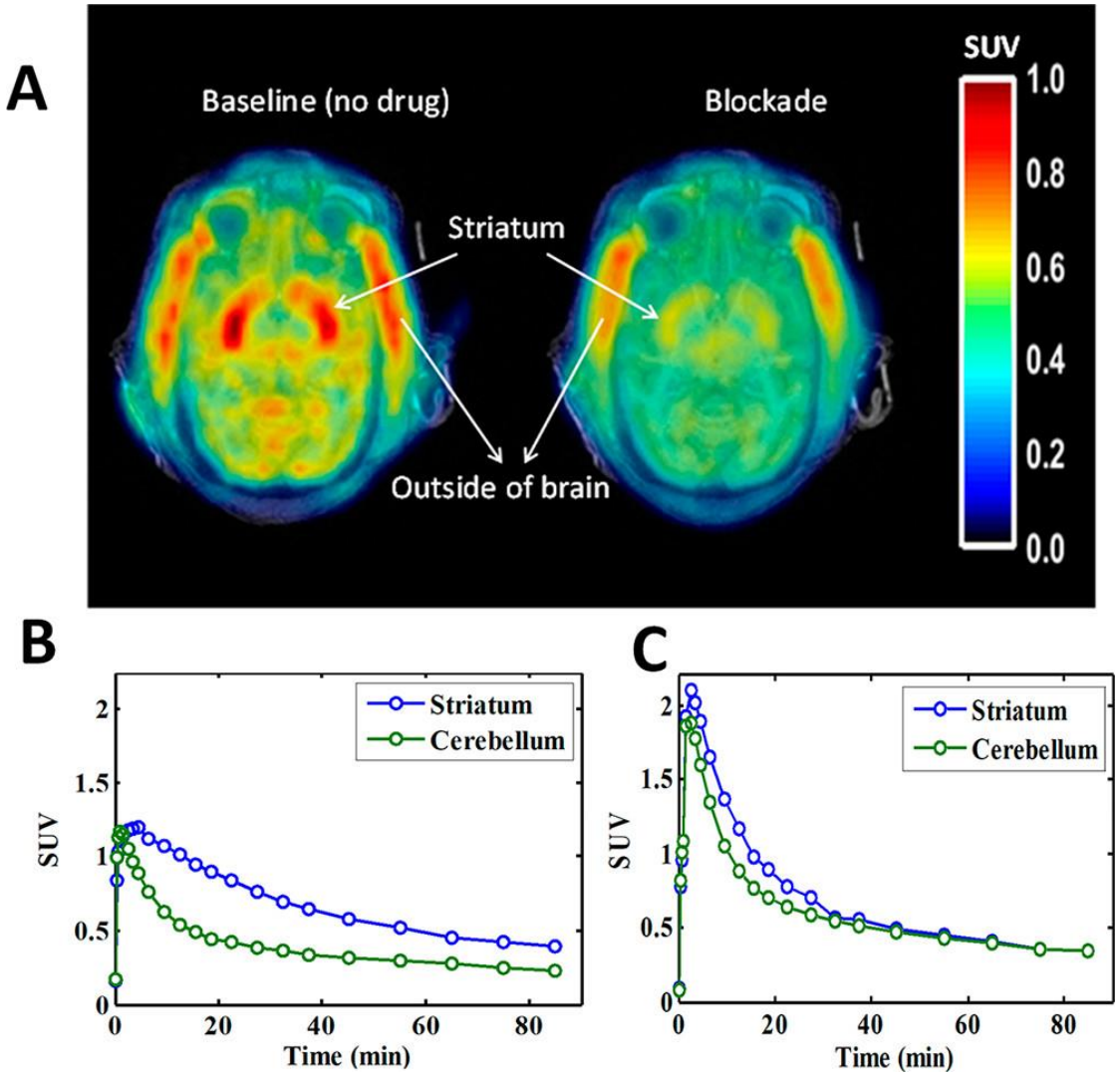
Source: Biomed Res. 2012 Mar; 26(2): 69–76.

In vitro Shift of Acetylcholine Potency with CVL-231



- CVL-231 increases activity of acetylcholine at M4 receptor by its positive allosteric modulation
- At clinically relevant concentrations, the increase in acetylcholine potency increases approximately 5- fold

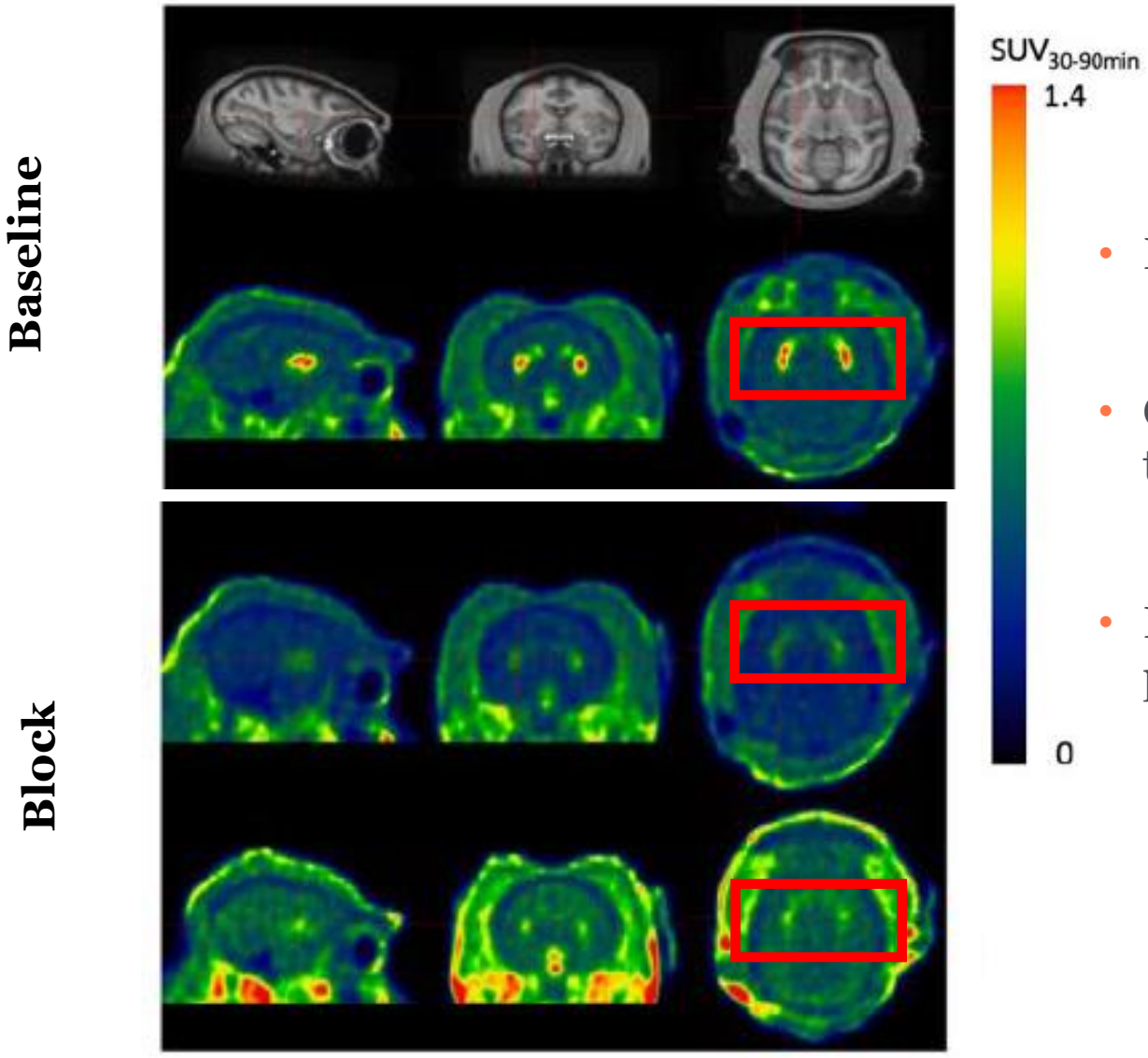
MK-6884 : Ligand for imaging M4 PAMs



- MK-6884 has been used to image binding to test compounds to the M4 PAM site in both NHPs and humans
- MK-6884 binds to M4 receptors in the striatum and is displaced by test M4 PAM compounds

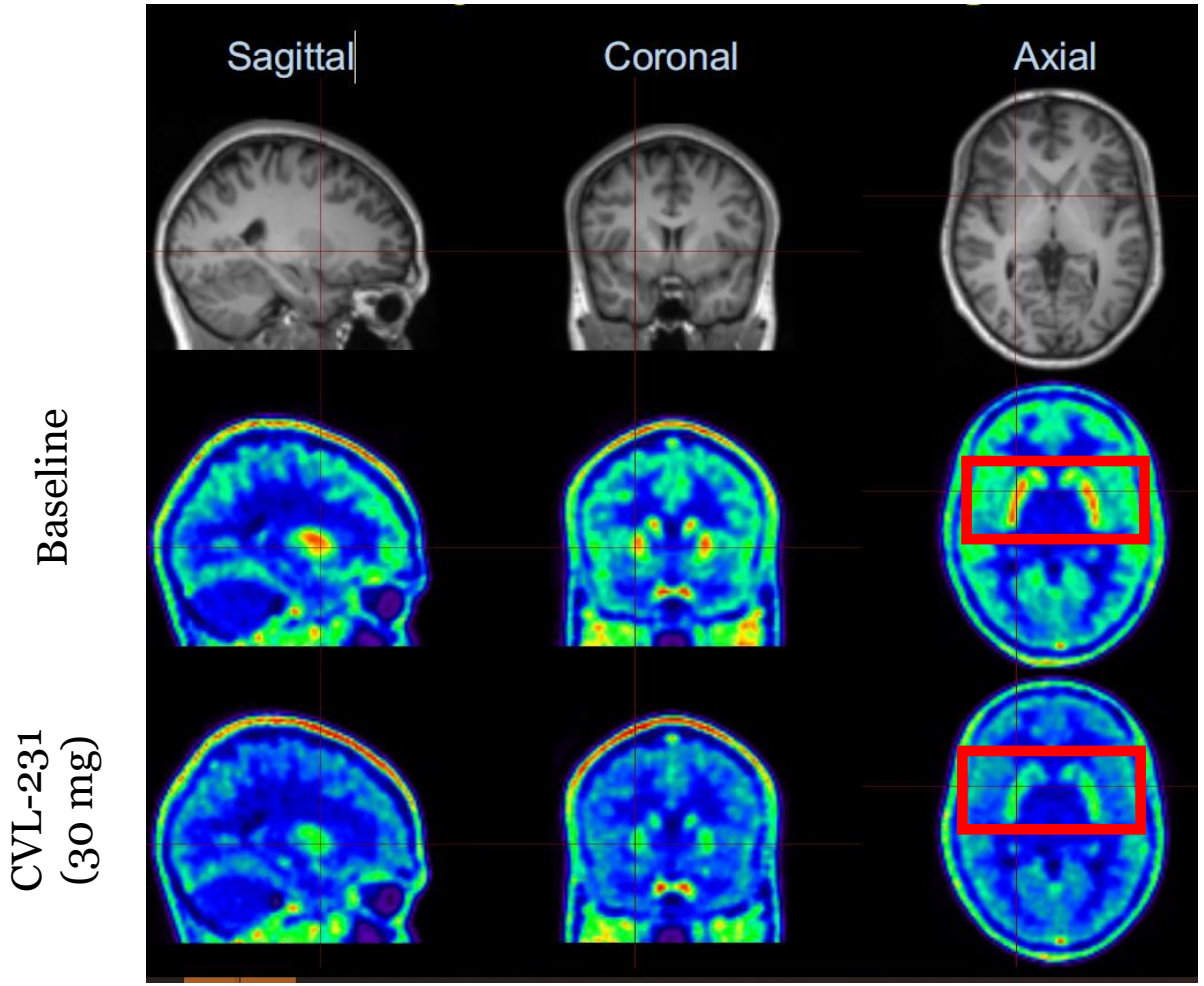
Source: J. Med. Chem. 2020, 63, 5, 2411–2425

Non-Human Primate Receptor Occupancy Data



- Doses tested ranged from 0.25 mg/kg - 1.7 mg/kg
- CVL-231 exposures in this dose range are similar to those attained in clinic
- PET RO studies in non-human primates enable projection of receptor occupancy curve in humans

Human PET RO Data to Date Consistent with NHP Study



- As predicted, at 30 mg dose CVL-231 displaces MK-6884 from M4 receptors in striatum
- Results of ongoing human PET RO studies will inform selection of low dose for Phase 2 to enable full dose-ranging trial

CVL-231: Next Steps

Our Plan for CVL-231

- One or more adequately-powered placebo-controlled Phase 2b trials to evaluate the full dose range for CVL-231 in schizophrenia
- Multiple dose arms, including 30 mg QD dose regimen
- Primary endpoint: Change from baseline on PANSS Total Score
- Six weeks in-patient treatment
- Patient profile similar to Phase 1b Part B
- Once-daily dosing
- No titration
- Full Phase 2 program details by mid to late Q1 2022

Q&A