ASX Announcement
13 October 2023

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Investor Presentation by Cogstate Executives

Cogstate (ASX.CGS) advises that senior executives of the company will be hosting a 90-minute investor briefing session on Friday 13 October at 11:00 AM Australian Eastern Summer Time.

DESCRIPTION
Investors are invited to register for a live webcast and Q&A hosted by CEO, Brad O'Connor. The briefing will be focused primarily on Cogstate's Clinical Trials business segment, which represents approximately 90% of Cogstate's current revenue base. Cogstate's clinical trials solutions include not only digital measures of cognition for use as an endpoint or screening tool in clinical trials, but also telehealth-style central rating and quality assurance services for study endpoints that combine innovative operational approaches, advanced analytics and clinical science expertise.

Presenters will include:

- **Rachel Colite, Executive Vice President Clinical Trials**. Rachel will provide an overview of the varied technology and services that Cogstate offers our pharmaceutical company customers.
- **Dr Chris Edgar, Chief Science Officer**. Chris will update investors on the significant recent developments in the field of Alzheimer's disease as well as likely trends that will impact Cogstate's business in coming periods.
- **Dr Pam Ventola, Vice President, Science**. Pam will discuss recent trends in rare disease clinical trials and why these approaches have become strategically important for many biotech companies.

Investors can register via the following weblink to join the live event or receive the recording if unable to attend: https://bit.ly/cogstate-investor-presentation

Additionally, a video recording of the presentation will be available following the presentation at the Cogstate Investor Centre homepage: https://www.cogstate.com/investors/.

A copy of the presentation materials is attached.

This announcement was authorised for release by Cogstate CEO, Brad O'Connor.

About Cogstate

Cogstate Ltd (ASX:CGS) is a leading neuroscience technology company optimising brain health assessments to advance the development of new medicines and to enable earlier clinical insights in healthcare. Cogstate technologies provide rapid, reliable and highly sensitive computerised cognitive tests across a growing list of domains and support electronic clinical outcome assessment (eCOA) solutions to replace costly and error-prone paper assessments with real-time data capture. The company's clinical trials solutions include quality assurance services for study endpoints that combine innovative operational approaches, advanced analytics and scientific consulting. For 20 years, Cogstate has proudly supported the leading-edge research needs of biopharmaceutical companies and academic institutions and the clinical care needs of physicians and patients around the world. In the Healthcare market, in August 2019 Cogstate entered into an exclusive licensing agreement with the pharmaceutical company Eisai, under which Eisai will market Cogstate technologies as digital cognitive assessment tools in Japanese markets. In October 2020, Cogstate extended its agreement with Eisai to the Rest of the World. The product, branded as NouKNOW, launched in Japan on 31 March 2020 (nouknow.jp). For more information, please visit www.cogstate.com.

For further information contact:
Brad O'Connor, Chief Executive Officer, boconnor@cogstate.com

Important Notices

Past performance

Past performance is given for illustrative purposes only and should not be relied upon as (and is not) an indication of Cogstate's views on its future financial performance or condition. Past performance of Cogstate cannot be relied upon as an indicator of (and provides no guidance as to) the future performance of Cogstate. Nothing contained in this announcement nor any information made available to you is, or shall be relied upon as, a promise, representation, warranty or guarantee, whether as to the past, present or future.

Future performance and forward-looking statements

This announcement contains certain "forward-looking statements". The words "expect", "anticipate", "estimate", "intend", "believe", "guidance", "should", "could", "may", "will", "predict", "plan" and other similar expressions are intended to identify forward-looking statements. Indications of, and guidance on, future earnings and financial position and performance are also forward-looking statements. Forward-looking statements, opinions and estimates provided in this announcement are based on assumptions and contingencies that are subject to change without notice and involve known and unknown risks and uncertainties and other factors that are beyond the control of Cogstate, its directors and management. Forward-looking statements are provided as a general guide only and should not be relied upon as an indication or guarantee of future performance.

Actual results, performance or achievements may differ materially from those expressed or implied in such statements and any projections and assumptions on which these statements are based. These statements may assume the success of Cogstate's business strategies, including the that the results of any of those strategies will be realised in the period for which the forward-looking statement may have been prepared or otherwise. For example, Cogstate's performance in any one financial period is sensitive to whether or not contracts are signed in that period, or a subsequent period, and the rate of enrolment in trials of its customers which are influenced by factors that are outside of Cogstate's control.

Readers are cautioned not to place undue reliance on forward-looking statements and except as required by law or regulation, none of Cogstate, its representatives or advisers assumes any obligation to update these forward-looking statements. No representation or warranty, express or implied, is made as to the accuracy, likelihood of achievement or reasonableness of any forecasts, prospects, returns or statements in relation to future matters contained in this announcement. The forward-looking statements are based on information available to Cogstate as at the date of this announcement. Except as required by law or regulation (including the ASX Listing Rules), none of Cogstate, its representatives or advisers undertakes any obligation to provide any additional or updated information, whether as a result of a change in expectations or assumptions, new information, future events or results or otherwise. Indications of, and guidance or outlook on, future earnings or financial position or performance are also forward-looking statements.

Cogstate Investor Presentation

Alzheimer's Disease Landscape | Rare Disease Landscape | Clinical Trials Capabilities

13 October 2023

Brad O'Connor
CEO

Chris Edgar, PhD
Chief Science Officer

Pam Ventola, PhD
VP, Science

Rachel Colite
EVP, Clinical Trials

BRAIN HEALTH FOR ALL

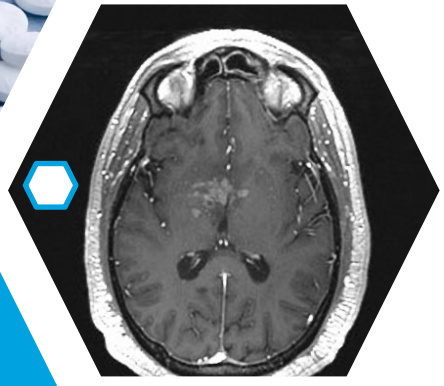
Cogstate

Alzheimer’s Disease Clinical Trials Landscape

Landmark Approvals with More Progress to Come

Tacrine approved by Food and Drug Administration (FDA) in 1993, donepezil 1996, rivastigmine 1998, galantamine 2001, and memantine 2003

Aduhelm 2022 and Lequembi 2023 first new FDA approvals in almost 20 years



Modest efficacy (≈30% slowing of progression), Amyloid-Related Imaging Abnormalities (ARIA) concerns, route of administration issues, limited access

- Approved therapies de-risk further investment.
- Further investment expected given modest efficacy and safety profile.

Revised Clinical Staging Criteria: Increasing Clarity Around Predementia Alzheimer's Disease (AD)

FDA Draft Early AD Guidance	NIA-AA 2018 Clinical Stages
Stage 1: Patients with characteristic pathophysiologic changes of AD but no evidence of clinical impact. These patients are truly asymptomatic with no subjective complaint, functional impairment, or detectable abnormalities on sensitive neuropsychological measures. The characteristic pathophysiologic changes are typically demonstrated by assessment of various biomarker measures.	**Stage 1:** • Performance in expected range, and • No reported cognitive decline (Cognitively unimpaired)
Stage 2: Patients with characteristic pathophysiologic changes of AD and subtle detectable abnormalities on sensitive neuropsychological measures, but no functional impairment. The emergence of subtle functional impairment signals a transition to Stage 3.	**Stage 2:** • Performance in expected range, and • Subjective cognitive decline, or • Documented evidence of decline, or • Newly acquired neurobehavioral symptoms (Cognitively unimpaired)
Stage 3: Patients with characteristic pathophysiologic changes of AD, subtle or more apparent detectable abnormalities on sensitive neuropsychological measures, and mild but detectable functional impairment. The functional impairment in this stage is not severe enough to warrant a diagnosis of overt dementia.	**Stage 3:** • Performance in impaired range, and • Cognitive decline from baseline in any domain, and • ADLs independent, but may be less efficient (Mild cognitive impairment)
Stage 4: Patients with overt dementia. This diagnosis is made as functional impairment worsens from that seen in Stage 3. This stage may be refined into additional categories (e.g., Stages 4, 5, and 6, corresponding with mild, moderate, and severe dementia) but a discussion of these disease stages is not the focus of this guidance.	**Stage 4:** • (Mild dementia) Substantial cognitive impairment affecting several domains, and • Clearly evident functional impact on daily life, and • No longer fully independent (Dementia) *Jack et al, Alzheimer's Dement. 2021*
Stage 5: Moderate dementia	N/A
Stage 6: Severe dementia	N/A

Measurement concepts:

- Biomarkers of Amyloid, Tau, and Neurodegeneration (ATN)
- Subjective cognitive decline
- Objective and subjective cognitive change (longitudinal)
- Objective cognitive impairment (cross-sectional Vs norms)
- Neurobehavioral symptoms
- Activities of Daily Living / Function
- Independence

Clinical Trials Landscape

How to increase effectiveness and access?

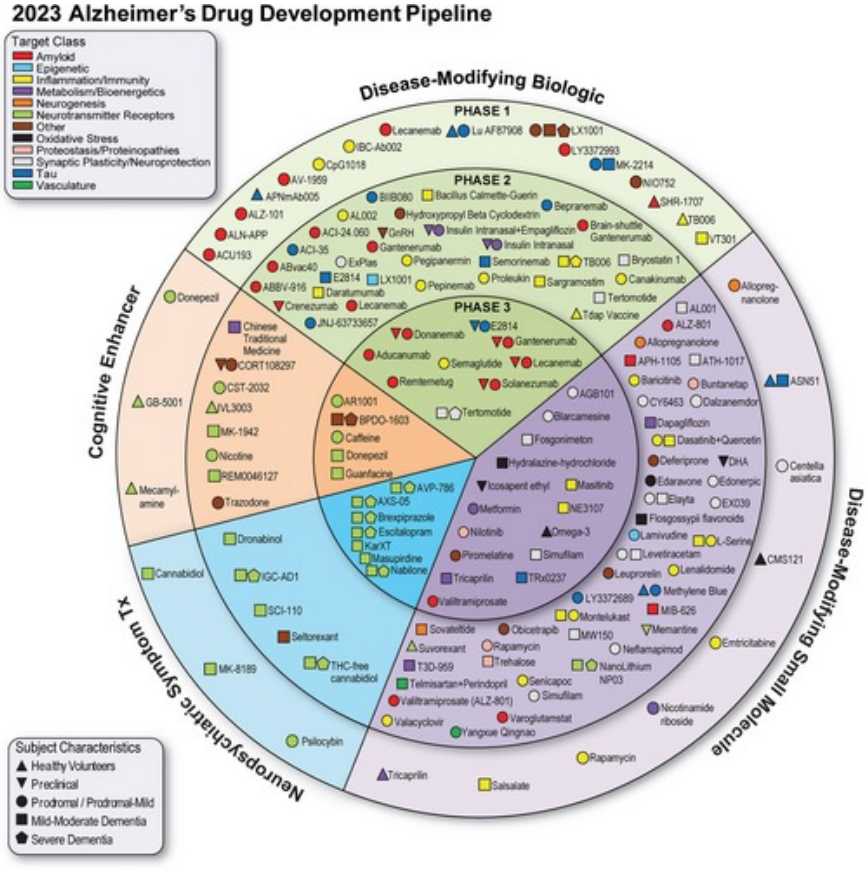
- Investigation of non-amyloid mechanisms of action (combination therapy)
- Routes of administration not requiring infusion or fewer infusions
- Reduced safety issues (ARIA) or ARIA preventing mechanisms
- Blood-based biomarkers
- Healthcare system improvements
- Treating earlier in the disease course

Active Research Area

- As of January 1, 2023,
- 187 trials assessing 141 unique treatments for AD
- Phase 3 included 36 agents in 55 trials
- 87 agents were in 99 Phase 2 trials
- Phase 1 had 31 agents in 33 trials
- Disease-modifying therapies were the most common comprising 79% of drugs in trials
- Populating all current Phase 1, 2, and 3 trials will require 57,465 participants

Cummings et al, 2023

Preclinical AD: An Opportunity for Disease Modifying Therapies



Cummings et al, Alzheimer's Dement. 2023

Prevention trials in patients with pathophysiologic changes of AD and no or only subtle cognitive abnormalities

- **Opportunities**
  - Larger market
  - Greater potential effectiveness
- **Challenges**
  - Larger sample size
  - Longer trial
  - Higher screen failure rate
  - Unsuited to Proof of Concept (PoC)

Decentralized Clinical Trials (DCT) in Preclinical AD

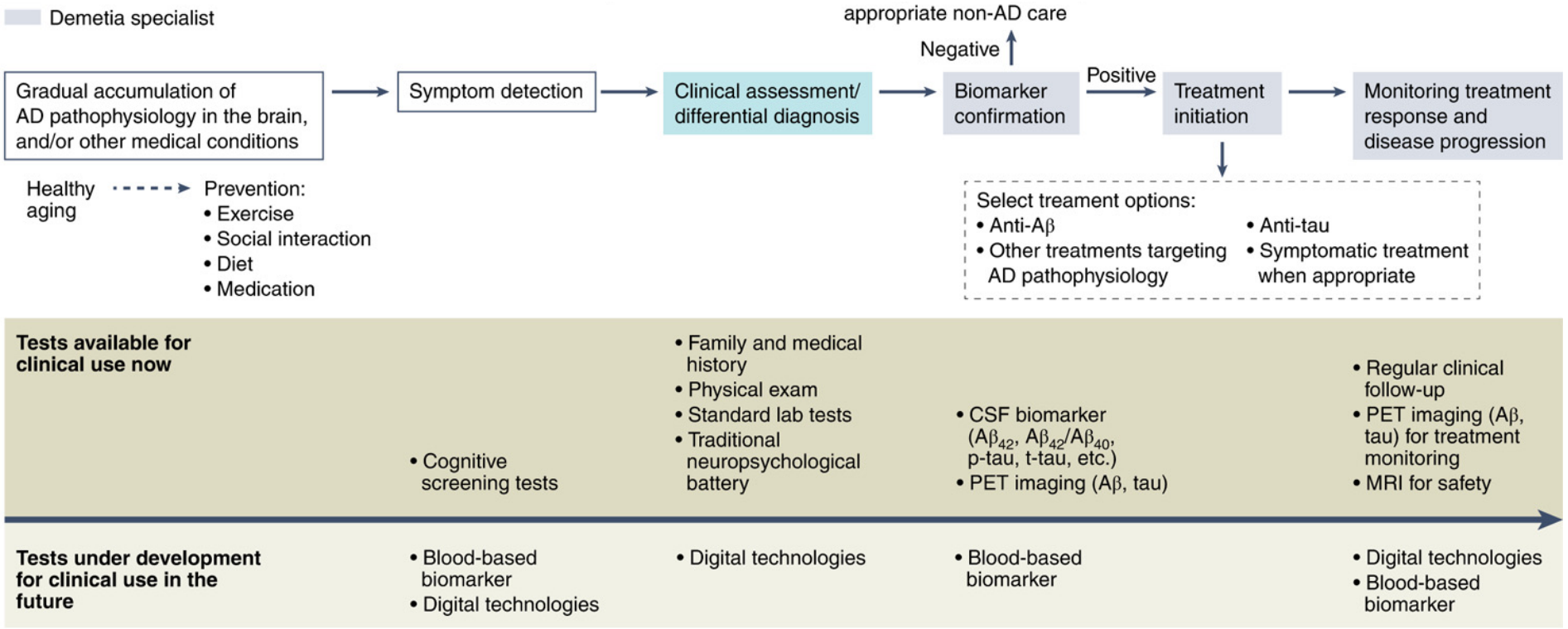
- Patients and study partners are younger and more cognitively able to engage with DCT technology
- Longer trial duration and greater likelihood of work commitment drives need to lower patient burden
- Increased concerns regarding recruitment and retention drives need to lower patient burden and increase site participation
- Relevant clinical outcome assessments (COAs) more amenable to remote and unsupervised contexts
- Central rating of COAs has the potential to reduce site burden/increase site participation and increase data quality

Greater flexibility in study design and conduct

Lower participant burden for improved recruitment/retention

Central rating to increase site participation and improve data quality

Multiple Opportunities for Digital Tools to Address Challenges



Hampel et al, Nat Aging 2022

Rare Disease Clinical Trials Landscape

What is a Rare Disease?

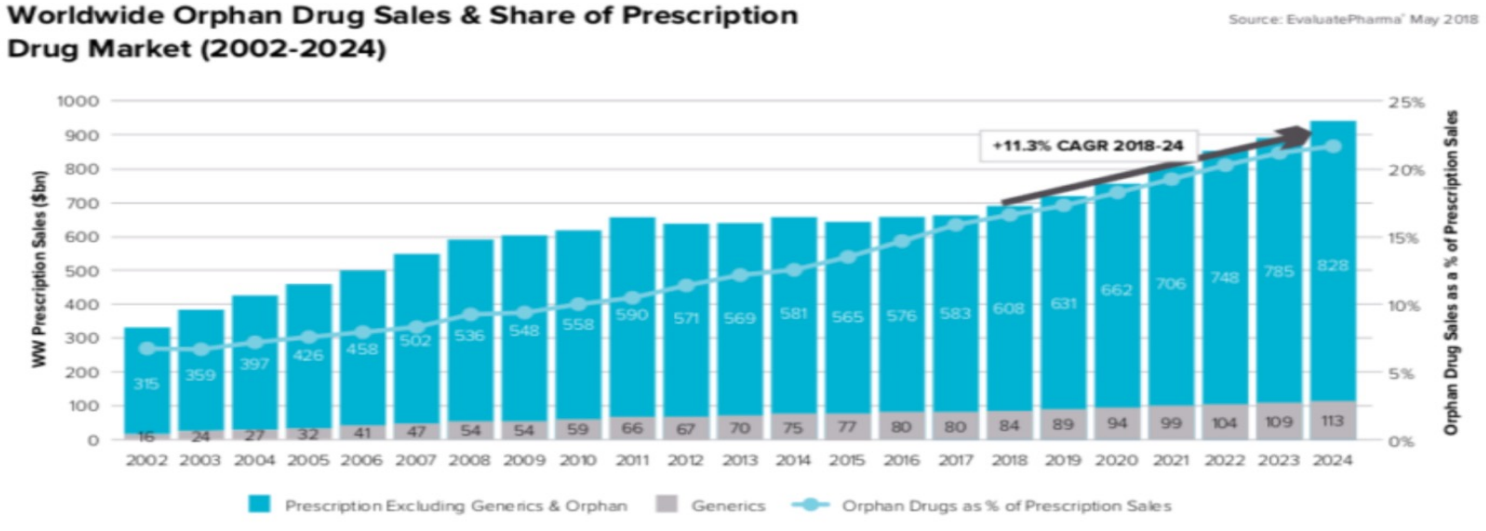
- **Rare Disease:**
  Affects less than 1 in 2,000 people
- **Ultra-Rare Disease:**
  Affects less than 1 in 50,000

Central Nervous System Rare Disease Examples

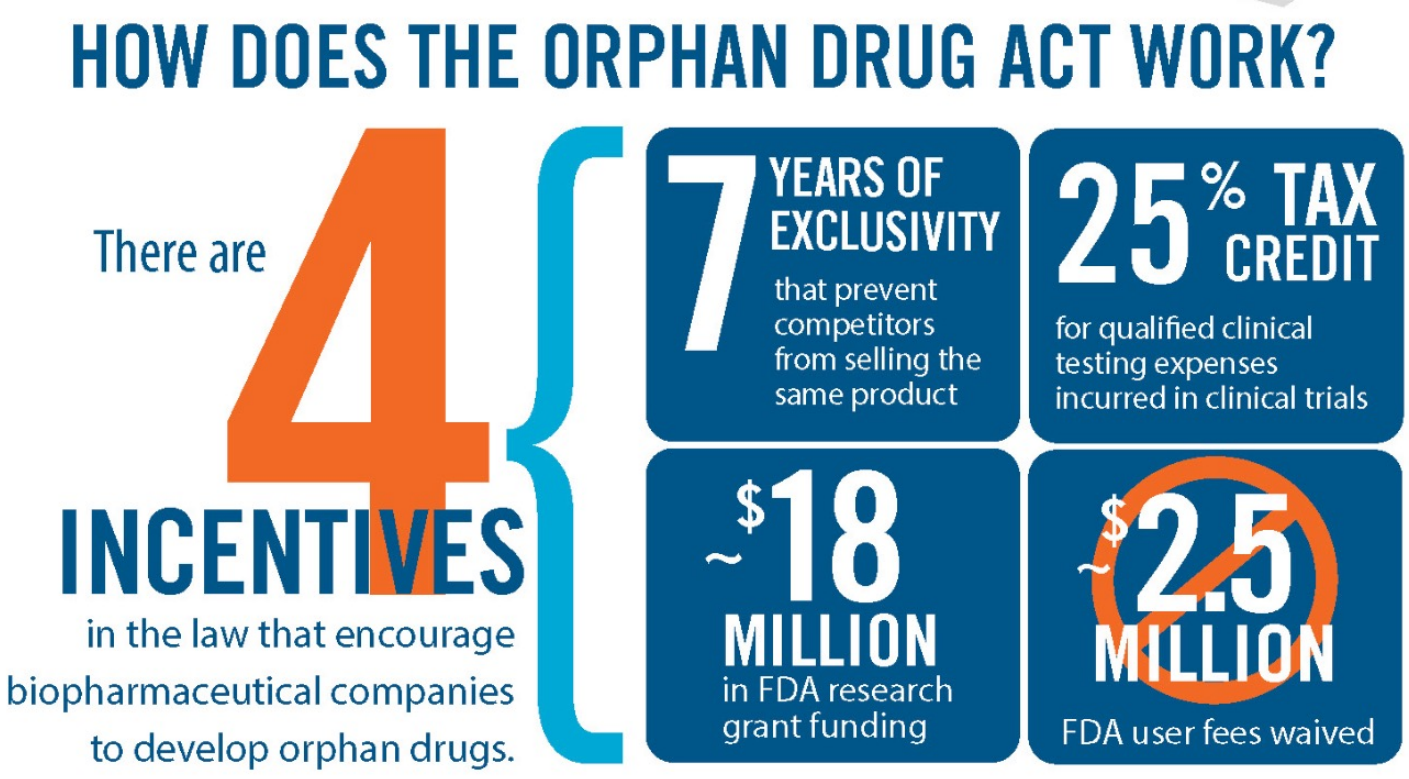
- Angelman syndrome
- Autism spectrum disorder
- Batten disease
- CDKL5 deficiency disorder
- Down syndrome
- Dravet syndrome
- Epileptic Encephalopathies
- Fragile X syndrome
- Hemophilia
- Lennox-Gastaut syndrome
- Mucopolysaccharidosis disease
- Mitochondrial disorders
- Tuberous Sclerosis complex
- And more

Why is Rare Disease an Attractive Market?

- In the 1970s, only 10 orphan drugs were approved.
- Between 1983 until 2019, there were 564 orphan drugs approved by the FDA.

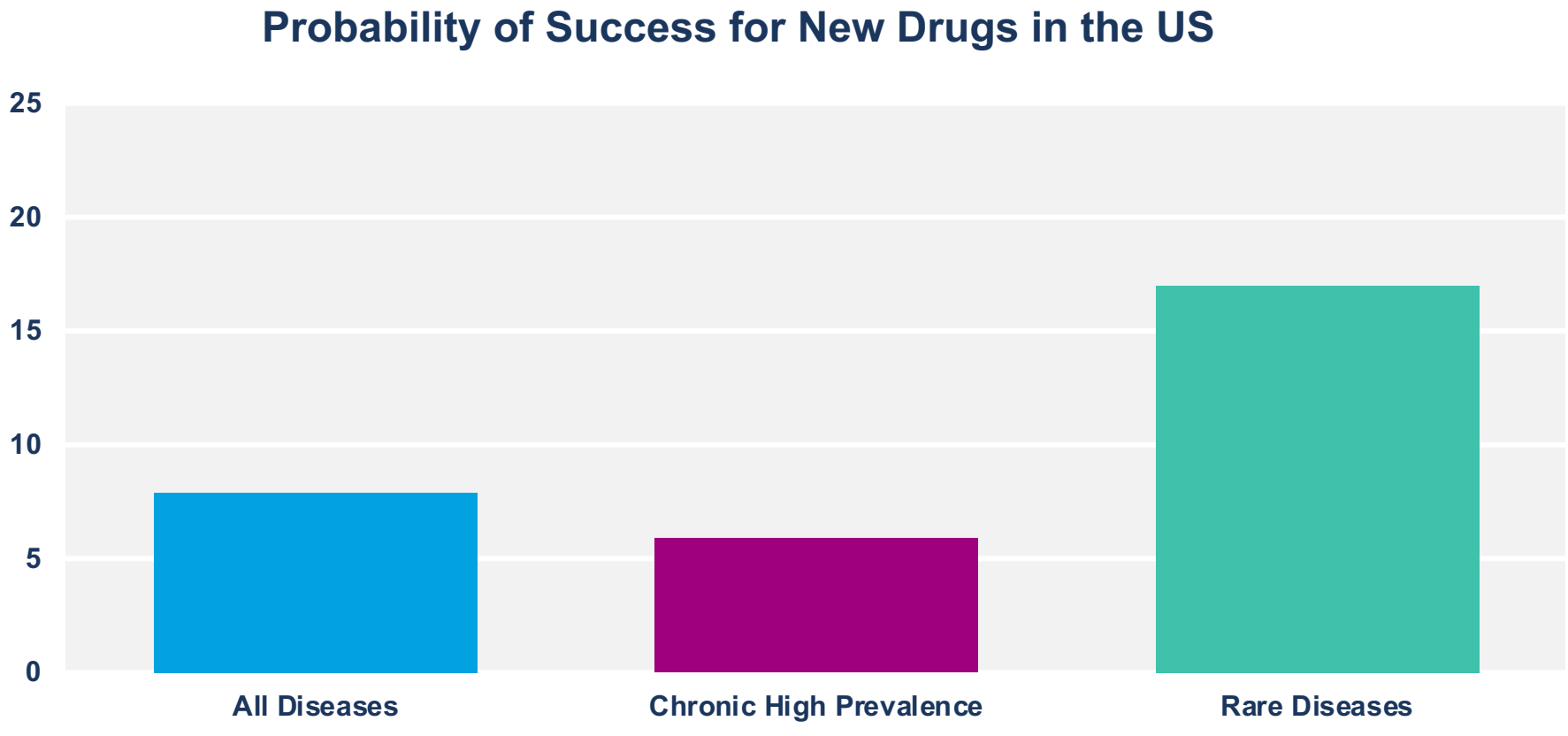


Focus on Rare



Accelerated Approval for Rare Disease Trials

Focus on Rare



Biotech Strategy

Moving Forward Strategically and Quickly

Strategy for Biotechs

- One compound can target multiple diseases
- One pivotal trial; multi-phase trials (combine Ph2/3 into one study)
  - Serious diseases with no treatment

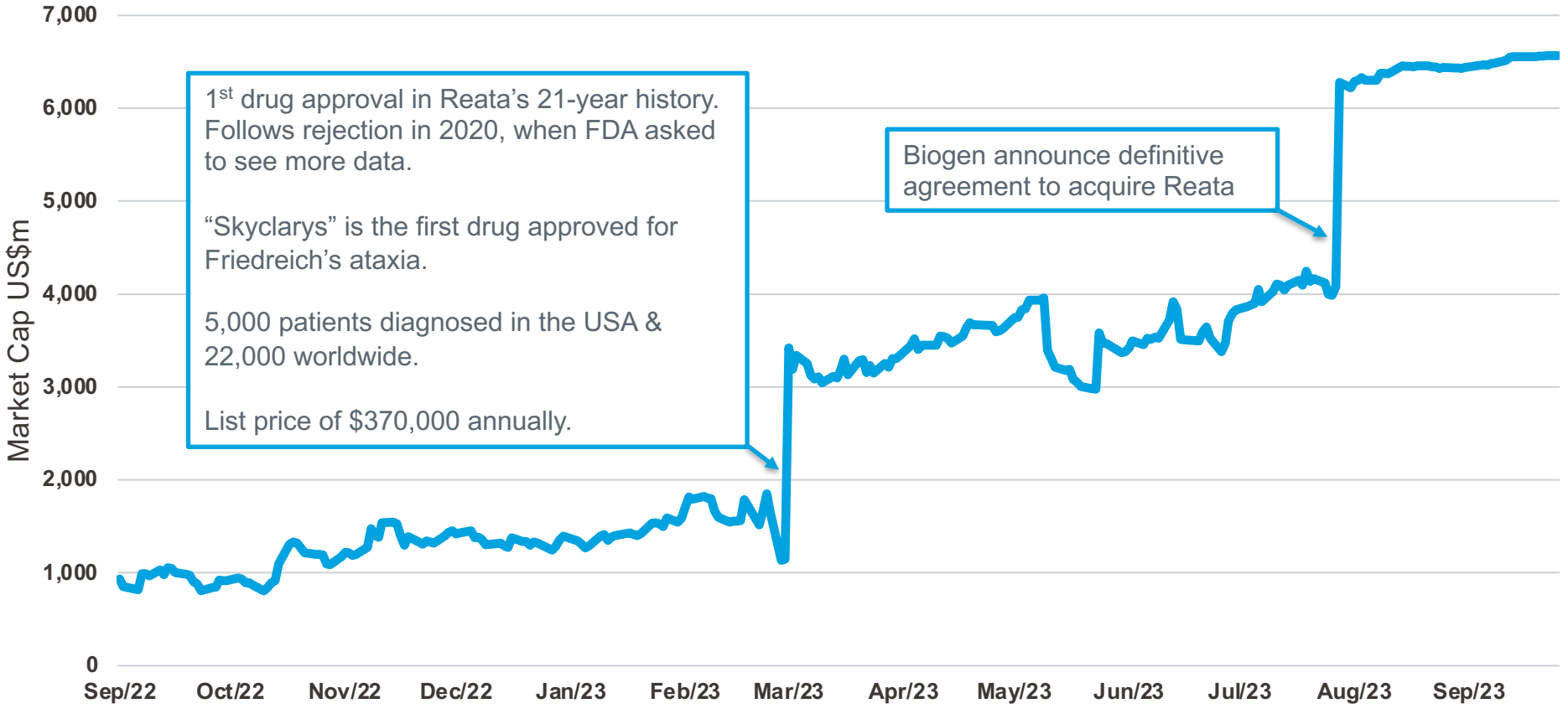
- Biotechs are able to move quickly and with agility, often because they are small companies
  - Risk/benefit ratio considerations
  - Decisions often driven by aggressive timelines

Recent Rare Disease Success

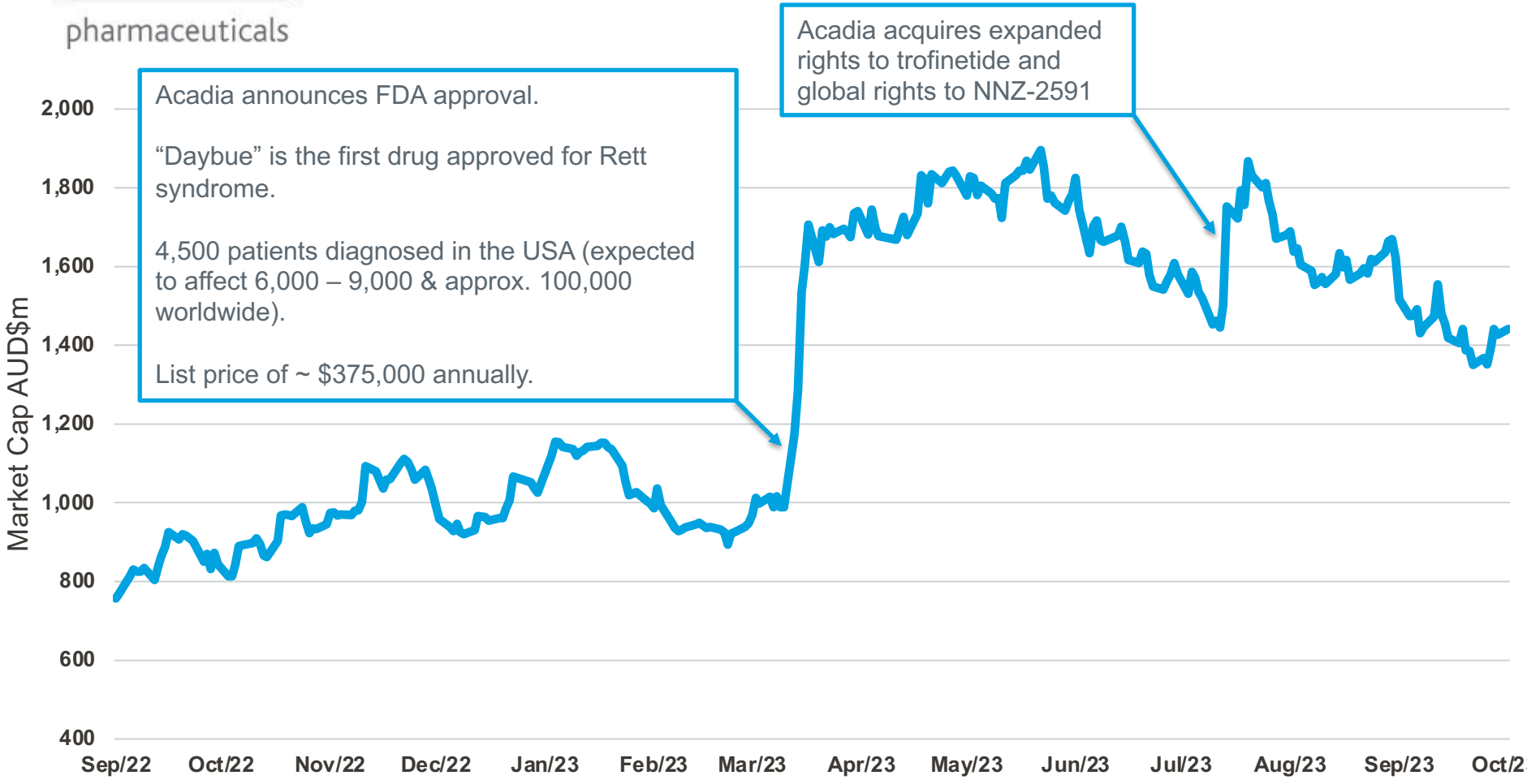
First Approval of Rare Genetic Neurological Disease

Trofinitide: Rett Syndrome

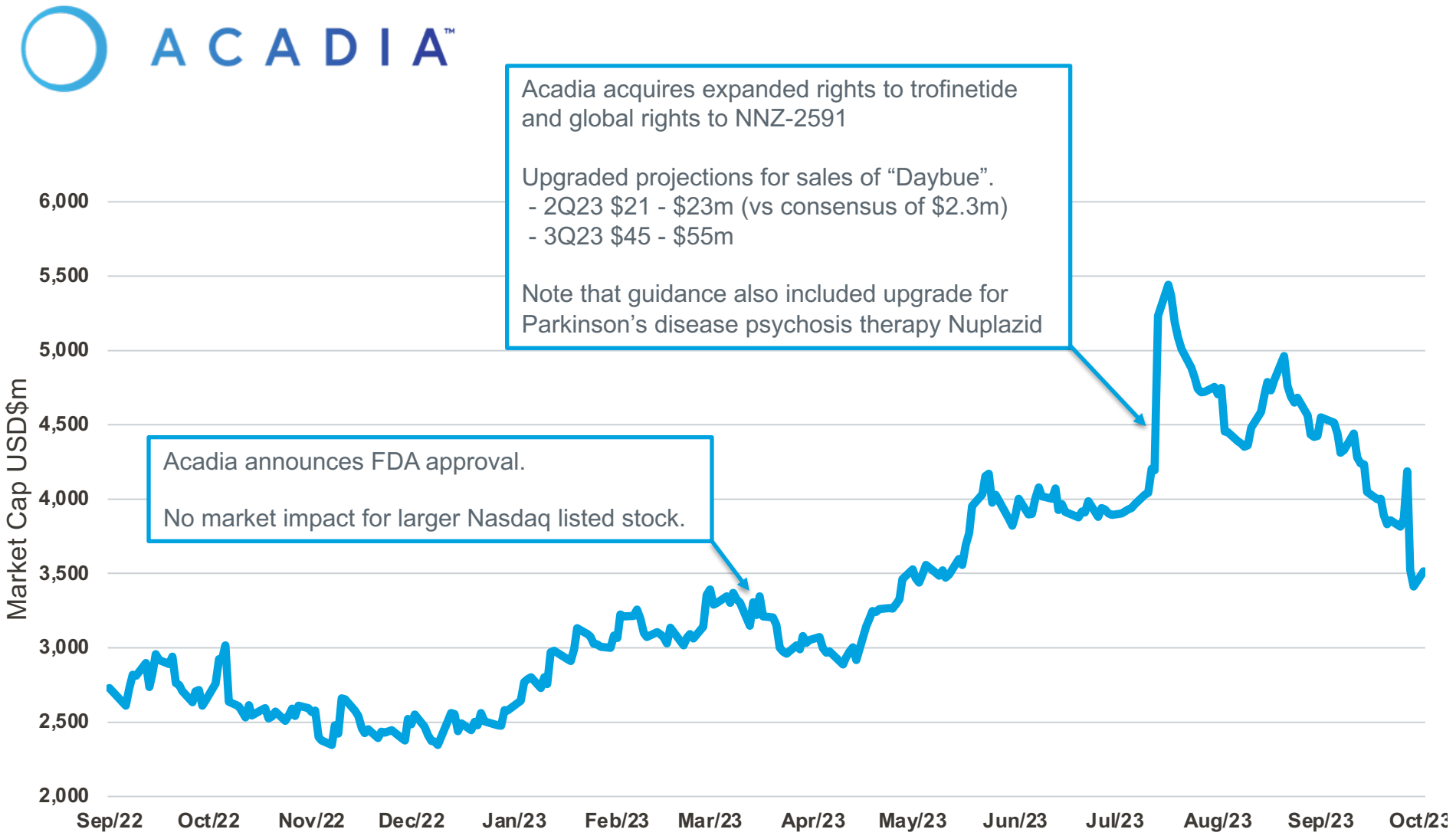
- Neuren licensed compound to Acadia
- Cogstate authored publication with Acadia providing evidence for the clinical meaningfulness of the change seen in the trial


7,000
6,000
5,000
4,000
3,000
2,000
1,000
0
Market Cap US$m
Sep/22
Oct/22
Nov/22
Dec/22
Jan/23
Feb/23
Mar/23
Apr/23
May/23
Jun/23
Jul/23
Aug/23
Sep/23
1st drug approval in Reata's 21-year history. Follows rejection in 2020, when FDA asked to see more data.
"Skyclarys" is the first drug approved for Friedreich's ataxia.
5,000 patients diagnosed in the USA & 22,000 worldwide.
List price of $370,000 annually.
Biogen announce definitive agreement to acquire Reata

neuren pharmaceuticals



ACADIA™


Acadia acquires expanded rights to trofinetide and global rights to NNZ-2591
Upgraded projections for sales of “Daybue”.
- 2Q23 $21 - $23m (vs consensus of $2.3m)
- 3Q23 $45 - $55m
Note that guidance also included upgrade for Parkinson’s disease psychosis therapy Nuplazid
Acadia announces FDA approval.
No market impact for larger Nasdaq listed stock.
Market Cap USD$m
6,000
5,500
5,000
4,500
4,000
3,500
3,000
2,500
2,000
Sep/22
Oct/22
Nov/22
Dec/22
Jan/23
Feb/23
Mar/23
Apr/23
May/23
Jun/23
Jul/23
Aug/23
Sep/23
Oct/23

Why Rare Disease for Cogstate

- Vast experience (~40 trials, across 25 indications)
- Natural History Studies experience
- Development of indication-specific outcome measures
- No clear precedence for measures or methodology
- Fast fail/ fast approval
    - Iterate on multiple smaller trials- scales easily

What sets us apart:

High-level and specialized scientific expertise and experience

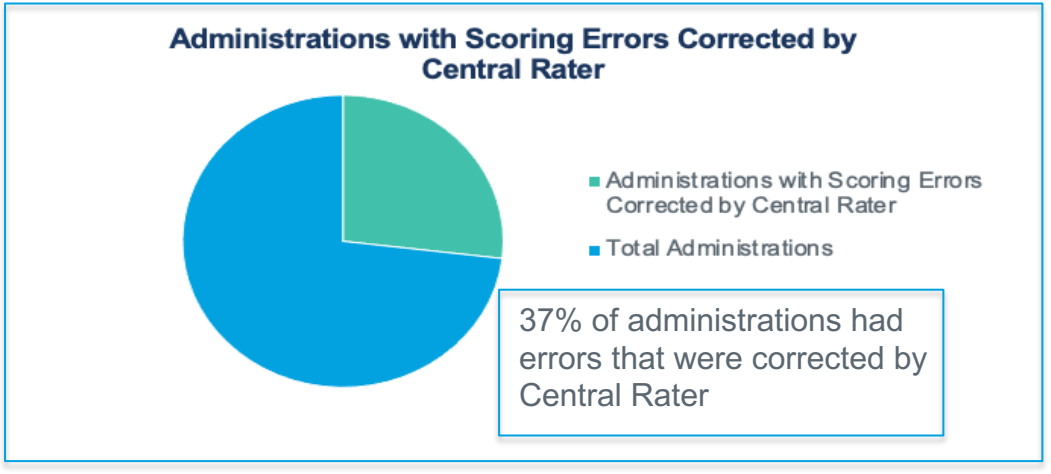
Why Rare Disease for Cogstate

Expertise in Natural History Studies

- Natural course of disease; Inform endpoints; Control condition of a treated group (that is, can replace the need for a placebo group)
- Cogstate currenting supporting four natural history studies
    - Example: Loulou Foundation (CDKL5 Deficiency Disorder)
        - 7 pharmaceutical partners
        - Natural history study results will be available to these 7 companies for future trials

Why Rare Disease for Cogstate

Central Rating and Central Scoring: Reduces Error and Decreases Site Burden



Use of Central Raters improves accuracy; reduces variance; increases efficiency

Recent Publications in Rare Disease

brain sciences

MDPI

Review

Clinical Development of Targeted Fragile X Syndrome Treatments: An Industry Perspective

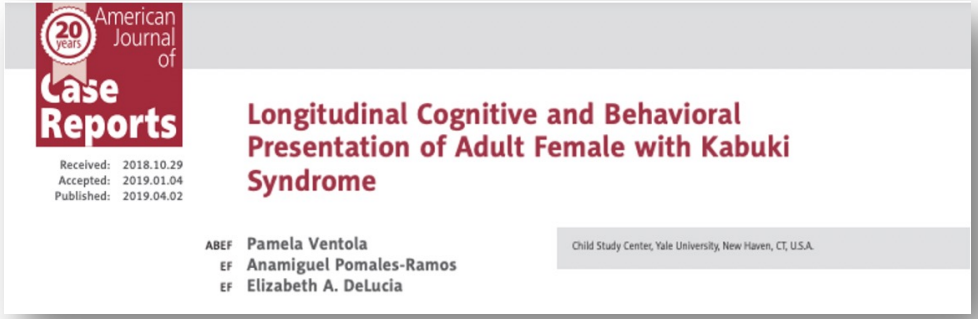
Anna W. Lee [1,*], Pamela Ventola [2], Dejan Budimirovic [3], Elizabeth Berry-Kravis [4] and Jeannie Visootsak [1]

RESEARCH ARTICLE

Adaptive Behavior in Autism: Minimal Clinically Important Differences on the Vineland-II

C. H. Chatham, K. I. Taylor, T. Charman, X. Liogier D'ardhuy, E. Eule, A. Fedele, A. Y. Hardan, E. Loth, L. Murtagh, M. del Valle Rubido, A. San Jose Caceres, J. Sevigny, L. Sikich, L. Snyder, J. E. Tillmann, P. E. Ventola, K. L. Walton-Bowen, P. P. Wang, T. Willgoss, and F. Bolognani

Autism Spectrum Disorder (ASD) is associated with persistent impairments in adaptive abilities across multiple domains. These social, personal, and communicative impairments become increasingly pronounced with development, and are present regardless of IQ. The Vineland Adaptive Behavior Scales, Second Edition (Vineland-II) is the most commonly used instrument for quantifying these impairments, but minimal clinically important differences (MCIDs) on Vineland-II scores have not been rigorously established in ASD. We pooled data from several consortia/



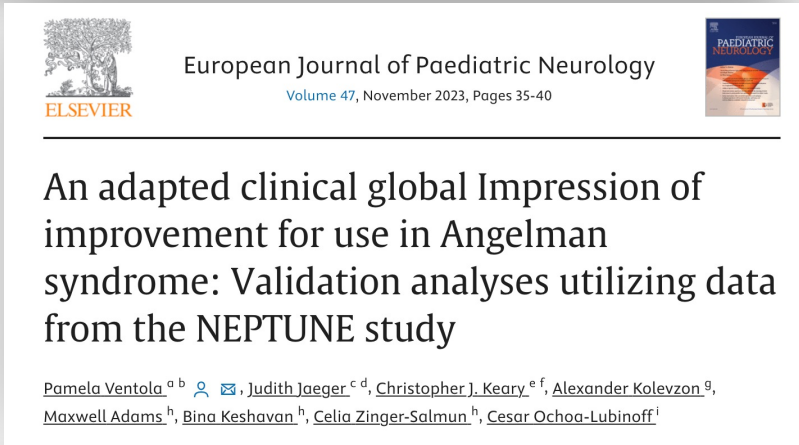
20 years American Journal of Case Reports

Received: 2018.10.29
Accepted: 2019.01.04
Published: 2019.04.02

Longitudinal Cognitive and Behavioral Presentation of Adult Female with Kabuki Syndrome

ABEF Pamela Ventola
EF Anamiguel Pomales-Ramos
EF Elizabeth A. DeLucia

Child Study Center, Yale University, New Haven, CT, U.S.A.



ELSEVIER

European Journal of Paediatric Neurology
Volume 47, November 2023, Pages 35-40

An adapted clinical global Impression of improvement for use in Angelman syndrome: Validation analyses utilizing data from the NEPTUNE study

Pamela Ventola [a b], Judith Jaeger [c d], Christopher J. Keary [e f], Alexander Kolevzon [g], Maxwell Adams [h], Bina Keshavan [h], Celia Zinger-Salmun [h], Cesar Ochoa-Lubinoff [i]

Ovid THERAPEUTICS BOLDMEDICINE

Methodology for Development of Indication-Specific Outcome Measures in Rare Disease Trials: An Innovative Research Approach

Pam Ventola[1,2], Anna Lee[3], Jeannie Visootsak[3]
1 Yale Child Study Center; 2 Cogstate; 3 Ovid Therapeutics

Cogstate

Clinical Trials Capabilities Overview

CNS Clinical Trial Vendor Ecosystem

1. Contract Research Organisations (CRO)
2. Clinical Trial Sites
3. Electronic Data Capture (EDC)
4. Electronic Clinical Outcome Assessment (eCOA)
5. Rater Training / Monitoring / Central Rating Organisations
6. Digital Assessments (Performance-based)
7. Other Digital Health Technologies (Remote Patient Monitoring and Wearables)

Other: Real World Evidence Organizations, Patient recruitment organisations, Electronic Trial Master File (eTMF) technology, Clinical Trial Management System (CTMS) technology , Electronic Health Record (EHR) data services, eConsent technology, RTSM / IRT, Televisit and scheduling technology, Translation organisations, Decentralized Research Organisations,

Cogstate brings together **clinical science expertise, innovative technology, and operational excellence** to help clinical trial teams understand drug safety and efficacy.

Scientific Consulting

Strategic guidance on the selection, execution and analysis of cognitive measures.

- Access to thousands of cognitive data profiles generated in different study populations, interventions, mechanisms
- Endpoint selection, powering decisions, robust statistical analysis and interpretation of study results supportive of product efficacy, safety and differentiating claims

Scale Management

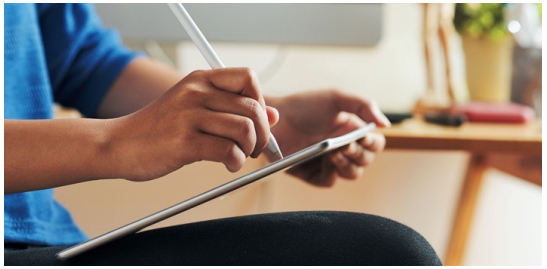
Licensing and translating rating scale instruments for a study is a meticulous process that can dramatically impact trial start-up timelines and data quality.

- Licensing agreements, translations and linguistic validation, development of master source documents
- Migration to electronic formats (eCOA)
- Logistics management of printed source, hardware, manipulatives and instructions

eCOA Solutions

Conventional paper and pencil assessments allow missing data and erroneous transcription. Electronic clinical outcome assessments (eCOA) allow for digital capture of study data with pre-set workflows, real-time edit checks and algorithmic flags to improve data quality.

- Patient-reported, clinician-reported, care partner-reported, performance-based
- Partner relationships



Rater Training

Clinical trial sponsors must ensure raters administer scales in the most accurate and standardized way possible.

- Prepare raters to administer scales to high standards in the timeliest way possible.
- Eliminate unnecessary training based on rater experience and leverage customized eLearning curriculum supportive of expedited study start-up.

Central Monitoring & Adjudication

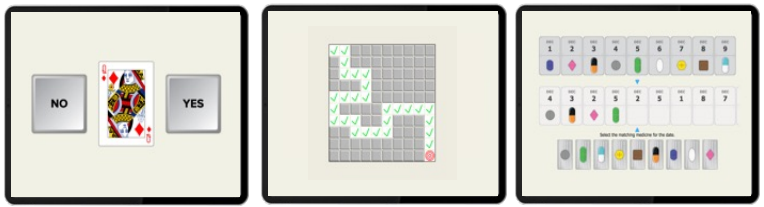
Rater variability and error can be detrimental to a study, adding noise and diminishing signal detection.

- Develop and execute strategic, risk-based central monitoring programs to ensure the reliability and validity of clinical measures.
- 200+ highly trained clinical and scientific experts who provide in-language support in 40+ languages.

Digital Cognitive Assessments

Increases the sensitivity and specificity of the measurement of human cognition.

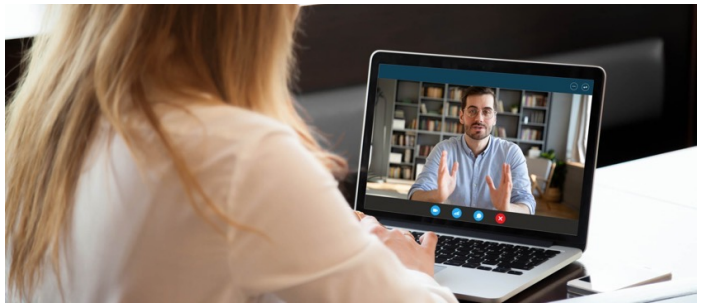
- Designed and validated to assess memory, verbal learning, attention, psychomotor function, motor function, executive function, vigilance, and emotional recognition
- Batteries are customized for the unique aims of each study -- used in hundreds of global clinical trials for both pediatrics and adults.



Remote Assessment

At-home data collection is increasing in Clinical Trials. Cogstate is expertly positioned to support remote administration of conventional clinical assessments as well as Cogstate proprietary digital assessments.

- Self-administered digital assessments
- Central rating via telehealth



Case Example:
Phase 3 AD Study

The need to enroll thousands of cognitively normal pre-clinical Alzheimer's participants meant innovative, patient-centric trial design was necessary (at-home cognitive assessment leveraging self-administered digital tests)

DETAILS

Phase 3 trial in participants with pre-clinical Alzheimer's disease

- Clinical Assessments
- Cognitive Assessments
- Patient-reported Outcomes

SERVICES

- Consulting
- Digital Cognitive Testing
- Rater Training
- Central Rating
- Central Monitoring

Dozens of highly experienced central raters vs hundreds of site raters

Cogstate