EXPANDED ACCESS SERIES (EAP)

Jinsy A. Andrews, MD, MSc, FAAN, FANA

Director of Neuromuscular Clinical Trials
Associate Professor of Neurology
Columbia University Irving Medical Center

Co-Chair, NEALS Consortium

HEALEY ALS PLATFORM
Weekly Webinar
EAP Series

MARCH 14, 2024

Healey & AMG Center
Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital
www.massgeneral.org/neurology/als.com

COLUMBIA | COLUMBIA UNIVERSITY IRVING MEDICAL CENTER

Objectives

1

Brief review of what is expanded access

2

Overview of ACT for ALS

3

Review of the NIH Funded CLENE Expanded Access Program (EAP)

Terminology for Preapproval Access

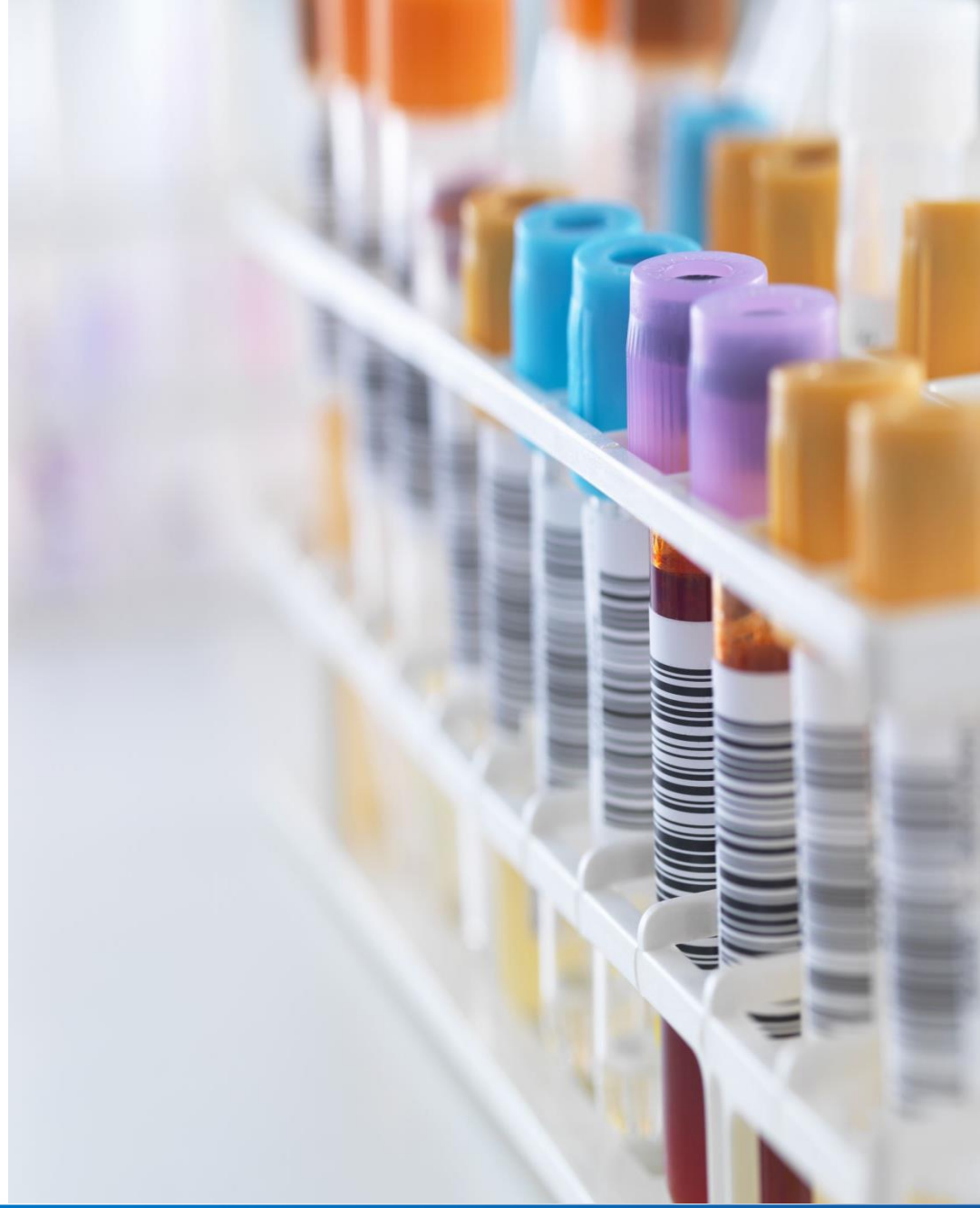
- **Clinical Trial:** any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes

- **Open label extension**: Typically, investigational product offered to clinical trial participants after completing the main portion of a controlled clinical trial

- **Off-label:** relating to the prescription of a drug for a condition other than that for which it has been officially approved

- **Expanded Access Program:** also called "*compassionate use,*" provides a pathway for patients to gain access to investigational drugs, biologics, and medical devices used to diagnose, monitor, or treat patients with serious diseases or conditions for which there are no comparable or satisfactory therapy options available outside of clinical trials

- **Right To Try:** U.S. state and federal laws that were created to let terminally ill patients try experimental therapies (drugs, biologics, devices) that have completed Phase I testing but have not been approved by the Food and Drug Administration (FDA)



When should you consider access to investigational therapy outside of a clinical trial?

- ❑ You have discussed and reviewed the risks and benefits of the FDA approved treatments with your healthcare team
- ❑ You are actively being cared for at a multidisciplinary ALS Center
- ❑ You have discussed and reviewed whether you need genetic testing for ALS with your healthcare team
- ❑ You reviewed all potential clinical trials and have been found not to be eligible for participation
- ❑ You have also considered alternative or off-label use of treatments, reviewed the rationale for considering in ALS and reviewed the risk/benefits with your healthcare team

About Expanded Access Protocols (EAPs)

U.S. FOOD & DRUG ADMINISTRATION

> *" a potential pathway for a patient with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available."*

An Expanded Access Protocol (EAP) can also be referred to as *Compassionate Use.*

Categories of FDA Expanded Access Drug Programs

FDA regulations describe general criteria, submission requirements and safeguards for these categories:

Individual Patient, including emergency use
[21 CFR 312.310]

Intermediate Size Patient Populations
[21 CFR 312.315]

Treatment IND or Treatment Protocol (widespread use or large patient population)
[21 CFR 312.320]

Expanded Access Program (EAP)

- Also referred to as ‘expanded access’, ‘treatment use’, or ‘compassionate use’
- Expanded access is regulated by FDA and provides investigational drug to certain eligible patients
- The primary objective of an expanded access drug program is to diagnose, monitor or treat patient’s disease or condition
- Traditionally, goal is not to obtain information about safety and effectiveness of the investigational drug
- *However, the ACT for ALS programs incorporate research goals in addition to providing access to investigational products in ALS*

ACT for ALS: Expanded Access Research for ALS

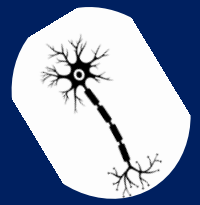
National Institute of Neurological Disorders and Stroke

The **Accelerating access to Critical Therapies for ALS Act,** commonly known as ACT for ALS, was signed into law on Dec. 23, 2021.

NIH NINDS

One of the several important initiatives is a **grant program that is administered by NINDS of the NIH**

Grant program intent: to **support scientific and clinical research** utilizing data from an intermediate-size Expanded Access Program **(EAP) for an investigational drug in ALS.**



Goal: To innovate the development of, and increase access to, potential new treatments for ALS.

What is included in ACT for ALS ?

- **GRANTS FOR RESEARCH ON THERAPIES FOR ALS** - creates a new grant program that funds access to investigational ALS treatments currently in development from small biotechnology companies for those patients who cannot participate in the clinical trial, while supporting research on how these investigational treatments impact the disease;
- **HHS PUBLIC-PRIVATE PARTNERSHIP FOR RARE NEURODEGENERATIVE DISEASES** - establishes an HHS Public-Private Partnership for Rare Neurodegenerative Diseases to advance the understanding of rare neurodegenerative diseases and foster the effective development and evaluation of treatments;
- **ALS AND OTHER RARE NEURODEGENERATIVE DISEASE ACTION PLAN** - commissions the publication of an FDA Action Plan to support drugs that improve and extend the lives of people as quickly as possible and facilitate access to investigational drugs for those living with amyotrophic lateral sclerosis and other rare neurodegenerative diseases.; and
- **FDA RARE NEURODEGENERATIVE DISEASE GRANT PROGRAM** - implements an FDA grant program to fund research and therapy development for ALS and other life-threatening or severely debilitating rare neurodegenerative diseases.

https://www.fda.gov/news-events/public-health-focus/accelerating-access-critical-therapies-als-act-act-als

CNM-Au8 | Surface Catalysis Improves Mitochondrial Function

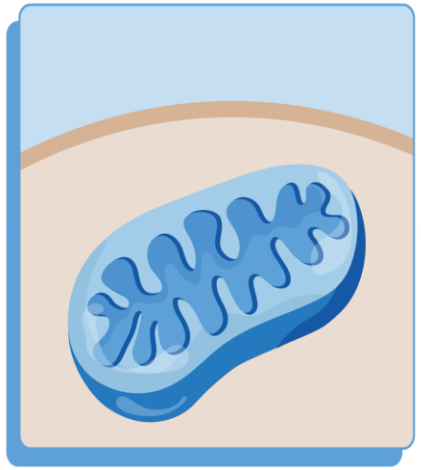
CNM-Au8 NANOCRYSTAL CATALYSIS

NAD+ ↑

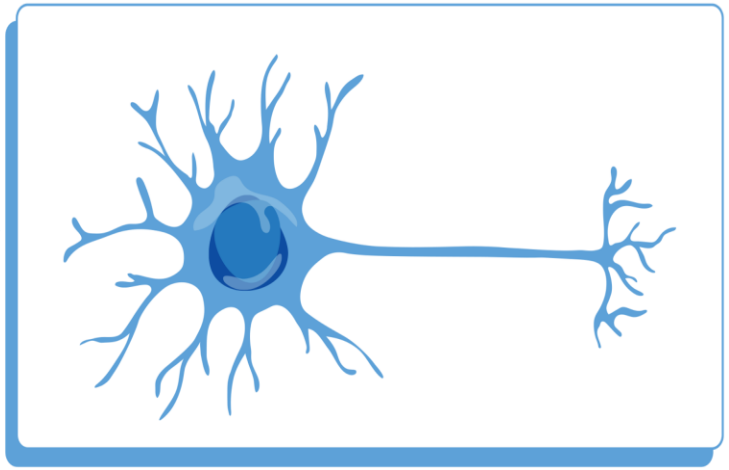
ROS ↓

Reactive Oxygen Species

MITOCHONDRIAL FUNCTION



NEURONAL SURVIVAL AND FUNCTION



Promising Evidence from Two Phase 2 Trials and Long-Term Data

CNM-Au8 Demonstrated Survival, Delayed Clinical Worsening, and Preserved Function

	RESCUE-ALS	RESCUE-OLE	HEALEY ALS Platform	HEALEY OLE	EAP
ALS Patient Demographics	Early-to-Mid-Stage (45)	Early-to-Mid-Stage	Mid-to-Late-Stage (161 Regimen C)	Mid-to-Late-Stage	Real-World Experience (256)
Duration	36-weeks	Up to 173 weeks	24-weeks	Up to 133 weeks	Over 4.0 years
Survival	--	✓	✓	✓ PRO-ACT	✓
Delayed Time to Clinical Worsening	✓	✓	✓	Pending data 1Q 2024	Not routinely collected
Preserved Function (ALSFRS-R)	--	✓	--		
Progression Biomarkers	p75 trend	↓ UCHL1 *	✓ NfL ↓	✓ NfL ↓	
Safety	>500 Years of Subject Exposure Without Identified Safety Signals Across ALS, MS, and PD				

CNMAu8.ACT-EAP | Objectives and Design

Objectives:

- To provide access to the investigational product, CNM-Au8, for ~140 participants diagnosed with ALS who are otherwise not eligible for current clinical trials.
- To evaluate safety and efficacy of CNM-Au8 treatment in ALS participants.

EAP STUDY DESIGN

Treatment Period:

- Up to 144 weeks of active treatment
- All participants will receive open label treatment with CNM-Au8 30mg orally or by feeding tube.
- Visits will be conducted on a recurring 12-week basis. Our EAP aims to strike a balance between the rigors of traditional clinical trial participation and the convenience of remote engagement. At some research clinics, specific 12-week visits will be required to be conducted onsite. For other 12-week visits, research clinics may be able to perform the visits virtually.
- Additionally, Clene is partnering with Synapticure, a specialty telehealth clinical care provider specializing in neurodegenerative diseases. For interested patients who may not reside near one of the participating research clinics, or those located in rural areas, completely virtual participation in this EAP is possible.

CNMAu8.ACT-EAP | Safety and Efficacy Assessments

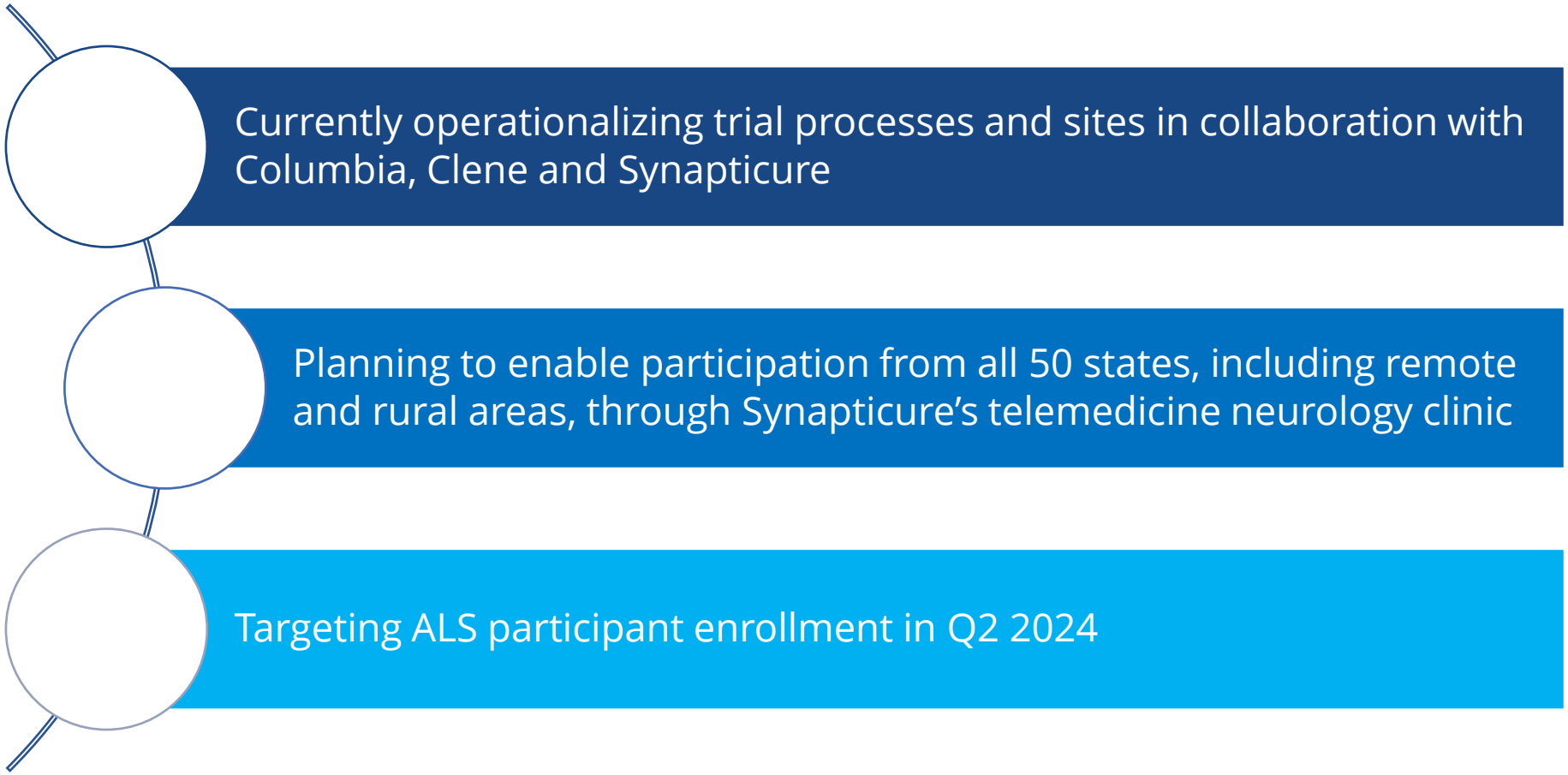
Safety will be monitored throughout the trial during study visits, including:

- **Collecting individual reports of changes in health**
- **Study event surveillance**
- **Assessing changes in individual's laboratory values**

Efficacy will be assessed using the data collected at each 12-week visit. Assessments performed at each visit may vary, but could include:

- **Breathing Assessments**
- **ALS Focused Questionnaires**
- **Blood Collection**
- **Medical/Safety Assessments**

CNMAu8.ACT-EAP | Current Status



In addition to this new EAP, Clene will continue to conduct its currently ongoing ALS EAP programs that have enrolled >250 participants since 2019.

THANK YOU!

Q&A