

# cyclo therapeutics

# Forward-Looking Statements

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The market data and certain other statistical information used throughout this presentation are based on independent industry publications, governmental publications, reports by market research firms or other independent sources. Some data are also based on the Company’s good faith estimates. In addition, this presentation includes summaries of scientific activities and outcomes that have been condensed to aid the reader in gaining general understanding.

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Factors that could cause the Company’s results to differ materially from those expressed in forward looking statements include, without limitation, the Company’s need for additional capital; the Company’s reliance on its Trappsol® Cyclo™ product, which may never receive regulatory approval; the Company’s ability to commercialize any of its proposed drug products if it receives regulatory approval; the outcome of the Company’s clinical trials, which may not support the Company’s product claims or may result in adverse side effects; the cost and timing of the Company’s clinical trials; the Company’s reliance on third parties to conduct clinical trials and to produce its products; and other risks associated with being a clinical stage biotechnology company.

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# Platform Technology Pipeline:

Trappsol® Cyclo™ allows for a multiple shots on goal model



Trappsol® Cyclo™

**Niemann-Pick Disease Type C**



**TransportNPC™**  
(Pivotal Phase 3 Study)  
Site activation ongoing and currently enrolling patients

Trappsol® Cyclo™

**Alzheimer's Disease**



Open IND for Phase 2 study

Orphan Drug Designation in U.S. | Fast Track Status in U.S. | Potential for Priority Review Voucher (PRV) in U.S  
Orphan Designation in EU | EMA Pediatric Investigational Plan Adopted

# Leadership Team with Proven Experience



N. Scott Fine  
Chief Executive Officer & Director



Joshua M. Fine  
Chief Financial Officer



Lise Lund Kjems, MD, PhD  
Chief Medical Officer



Michael Lisjak  
Chief Regulatory Officer



Jeffrey L. Tate, Ph.D.  
Chief Operating Officer, Chief Quality Officer & Director



Lori McKenna Gorski  
Global Head of Patient Advocacy



# Scientific Advisory Board



Rita Colwell, Ph.D.

Co-Chair

Internationally recognized scientist, microbiologist and founder of CosmosID, a privately held bioinformatics firm. Distinguished University Professor at U. Maryland and Johns Hopkins University. Former Director, National Science Foundation (1998 - 2006). National Medal of Science awardee. Member, US National Academy of Sciences.



Sharon H. Hrynkow, Ph.D.

Co-Chair

Neuroscientist with more than 25 years' experience in global health arena, public and private sectors. Senior executive at NIH. First president of non-profit Global Virus Network. Former Member of President's Council of Advisors on Science and Technology. 5 years at Cyclo Therapeutics leading clinical and scientific programs.



Benny Liu, M.D.

Key Opinion Leader in Niemann-Pick Disease Type C

Gastroenterologist at Alameda Healthy System, CA and Highland Hospital. Globally recognized expert in lipid metabolism. First to discover that cyclodextrins release cholesterol from cells using an animal model. Assistant Clinical Professor, UCSF.



Caroline Hastings, M.D.

Key Opinion Leader in Niemann-Pick Disease Type C

Pediatric hematologist oncologist, Director of NeuroOncology, and Professor of Pediatrics, UCSF Benioff Children's Hospital Oakland. First physician in US to use cyclodextrins for treatment in NPC, compassionate use. Advisor to US and Australian NPC Advocacy organizations and to physicians globally on NPC.



Gerald F. Cox, M.D., Ph.D.

Internationally Renowned for Clinical Drug Development

Seasoned biotechnology executive with 20-year successful track record of drug development for rare genetic diseases and extensive worldwide regulatory experience



# Niemann-Pick Disease Type C

Ongoing Pivotal **TransportNPC**<sup>™</sup>  
Phase 3 Study



# NPC: A Debilitating Disease with Fatal Outcomes

- Rare, fatal and progressive genetic disorder effecting the brain, liver, spleen and lungs.
- Characterized by a defect in the NPC1 protein
- Cholesterol and lipids accumulate in cells of major organs and tissues
- Leading to cell and tissue dysfunction

0 U.S. Approved NPC Therapies

1 EU Approved Therapy with no systemic effects

## Market Opportunity<sup>1</sup>

United States: \$300 Million | Worldwide: \$600 Million

### Incidences

1/100,000 (~35 per year in U.S.)

### Of Diagnosis

~ 3% are age 3 and below  
 ~ 97% are age 3 and above  
 ~ 60% age 16 and above

### Median Survival

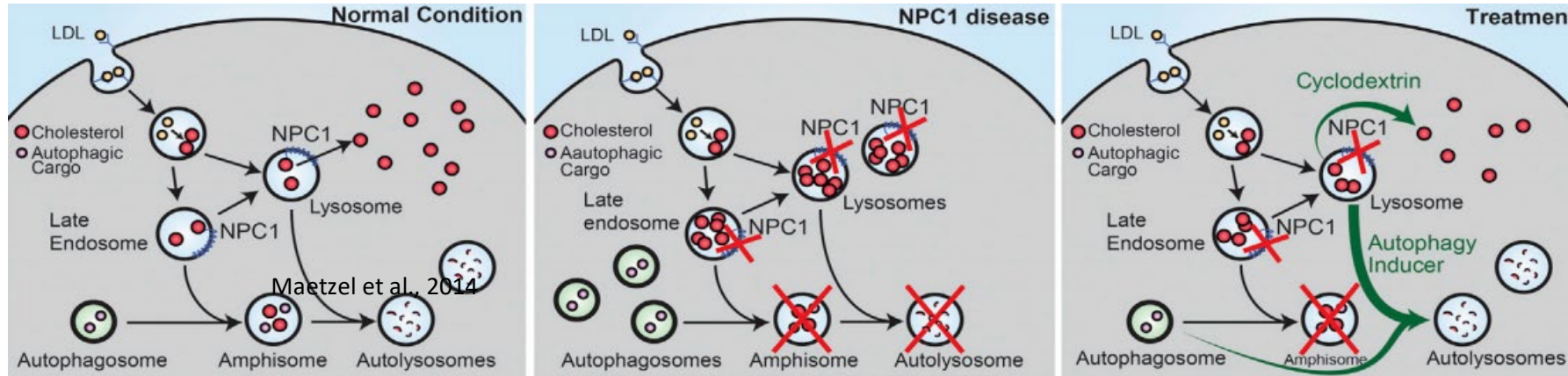
Early Infantile (2m-2): 4.6y  
 Late Infantile (3-6): 9.4y  
 Juvenile (7-15): 15.4y  
 Adolescent/Adult (16+): 12.2y

1: Data on file Cyclo Therapeutics

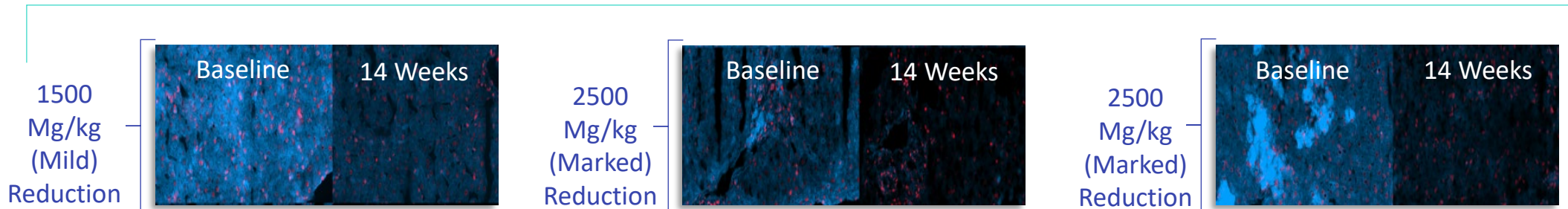
\*Scope: United States + 79 other countries; \*Commissioned Tessellon Inc – former Kantar Health experts with 25+ years of epidemiology and forecasting experience, ([www.Tessellon.com](http://www.Tessellon.com)); \*Exhaustive literature search with a broad range of MESH terms.

# Trappsol<sup>®</sup> Cyclo<sup>™</sup>

## Enables the Effective Transport of Cholesterol Out of Cells



Cholesterol as measured by Filipin staining at Baseline and after 7 doses over 14 weeks



The lack of light blue represents the clearing of cholesterol from cells

# Trappsol<sup>®</sup> Cyclo<sup>™</sup> Summary of Completed Clinical Studies in NPC

## Study 101

Phase 1 study in NPC patients age 18 years and older showed Trappsol<sup>®</sup> Cyclo<sup>™</sup> was well-tolerated with an acceptable safety and tolerability profile

- After IV infusion, the drug is detectable in the cerebrospinal fluid within hours after the start of infusion
- Cholesterol synthesis and metabolism affected, and cholesterol cleared from cells, mimicking effects from nonclinical studies (in vitro and in vivo) in NPC models

## Study 201























Consistent pharmacodynamic effects and safety profile observed in a 48-week Phase 1/2 study in NPC patients aged 2 years and older

- 100% of patients assessed by treating physicians to be either stable or improved
- 88% (8 of 9 patients who completed the study), experienced clinically meaningful improvements in one or more efficacy endpoints, assessed by the 17 Domain NPC Severity Scale
- Based on totality of data from the Phase 1 and Phase 2 studies, the 2000 mg/kg dose was selected for the Phase 3 study

Double-blind, Randomized, Placebo-controlled, Parallel-group study and is currently the most advanced clinical research program underway to identify a treatment for NPC

Number of Subjects	93
Current Sites	23 across 9 countries United States, United Kingdom, Italy, Germany, Spain, France, Poland, Israel, and Australia
Duration	96-week trial, with Interim Analysis at 48 weeks
Dose	2000 mg/kg via IV infusion
Primary Endpoint	NPC Composite Severity Score
Secondary Endpoints	SCAFI, Swallow, Vineland-2
Exploratory Endpoints	Inclusive of Speech, Liver and Lung function

# We Have the Only Active Late-Stage Clinical Program in NPC

Company	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Potential Indication (Systemic and Neurological)	Safety Profile	Summary
 cyclo therapeutics	Trappsol® Cyclo™ (Intravenous every 2 weeks, Home infusions)							Met all primary endpoints of the Ph1 and Ph1/2 showing favorable safety and efficacy. Ph3 currently enrolling and additional site activation ongoing.
 ACTELION	Zavesca* (Oral 3 times daily)							FDA: Data did not support benefit risk. Off-label in US. EMA: Approved January 2009.
ORPHA  ZYME	Arimoclomol (Oral 3 times daily)							FDA: CRL received June 18, 2021, noting additional data required to support benefit risk. EMA: CHMP Opinion and potential MAA anticipated Q1 2022 as Adjunct Therapy.
 IntraBio	IB1001 (Oral 3 times daily)							Met with FDA, EMA and UK, Phase 3 study required, 6-month placebo-controlled crossover trial with approximately 50 patients (4 years of age and above). Study enrollment anticipated H1 2022.
 Mandos Health	Adrabetadex (VTS-270) (Intrathecal every 2 weeks)							MNK concluded program 20-Jan-2021 noting the benefit risk is negative. Mandos received Court Approval to buy from MNK 29-Jun-2021. FDA has not found drug to be safe and effective for use to treat NPC1 or for any other use.
 ESCAPE BIO	ESB1609 (Oral, brain-penetrant)					TBD	TBD	Selective sphingosine-1-phosphate 5 (S1P5) receptor agonist.

# Alzheimer's Disease

Open IND for  
Phase 2 study



# Alzheimer's Disease

## The Most Common Form of Dementia

An irreversible, progressive neurologic disorder that slowly degrades memory, thinking and social skills that affects a person's ability to function independently.

### Similarities with NPC

Cognitive decline

Elevated levels of tau

Amyloid plaques

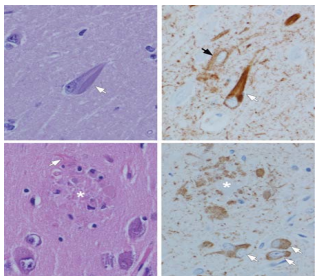


- Affects more than 5 million people in the U.S.<sup>1</sup>
- 6th leading cause of death in the U.S.<sup>1</sup>
- 500,000 new cases every year<sup>2</sup>
- 13.8 million cases projected by 2050<sup>1</sup>

# Commonality Across Target Neurodegenerative Diseases

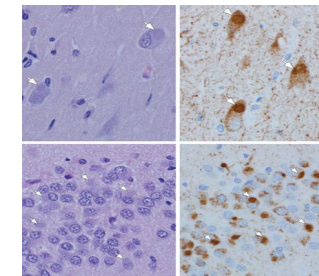
## Alzheimer's Disease

### Secondary Tauopathy



## Niemann-Pick Disease Type C

### Primary Tauopathy



### Biologic Similarities

Cholesterol Accumulation in Regions of Brain

Elevated Levels of Tau in CSF

Amyloid Plaques in the Brain

### Disease Manifestation

Cognitive decline / dementia

Premature death

Clumsiness

Progressive motor symptoms

Ataxia, dystonia, dysarthria, dysphasia

Psychiatric signs: psychosis, depression

Weight loss

### Disease Manifestation

Progressive cognitive decline / early dementia

Premature death

Clumsiness, gait disturbance

Delayed motor milestones

Progressive: ataxia, dystonia

Seizures

Weight loss

# Trappsol® Cyclo™ for the Potential Treatment of Alzheimer's Disease Targeting Reduction of Amyloid Beta and Tau

Received IND Clearance from the U.S. FDA to Advance Phase 2 Study

Preeminent Neuroscientist and World-Renowned Researcher,  
Cynthia A. Lemere, PhD Senior Advisor for Advancement of Alzheimer's Disease Asset

## Positive Results in Alzheimer Patient Under Compassionate Use Program

FDA authorized use of Trappsol® Cyclo™  
in geriatric patient

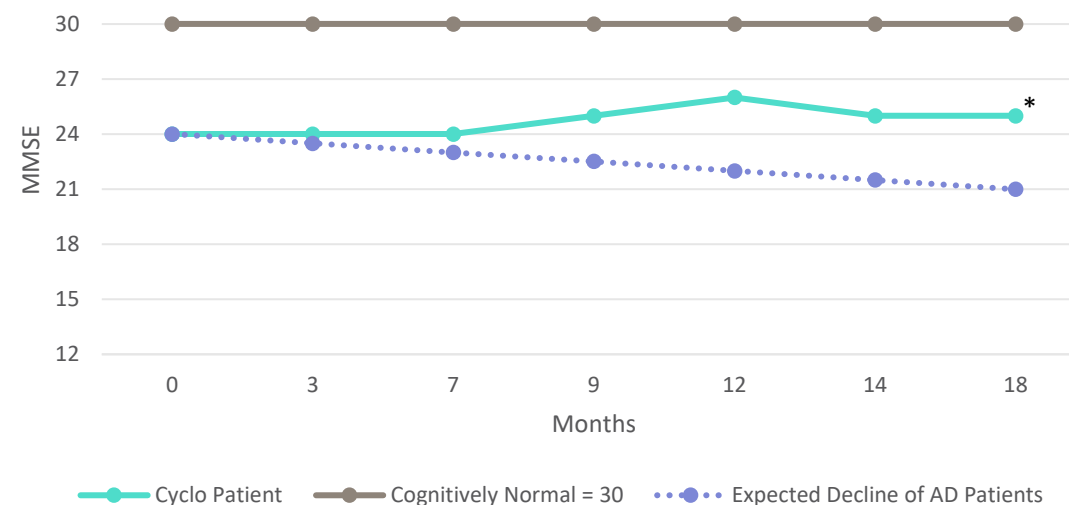
18 months of monthly IV infusion

Disease did not progress

Family reported less volatility and greater word-  
finding ability

18 months of data has led to development  
of Phase 2 protocol

### Alzheimer's Mini-Mental State Evaluation Performance<sup>1</sup>



*"The patient has shown cognitive and neurologic stability in serial examinations during this study that indicates possible benefit as there would be an expected measurable cognitive and functional decline over an 18-month period in persons with Alzheimer's disease dementia,"* Treating Physician

\*Treating physician reported the 18-month score as a range between 24-26

1: Rate of MMSE decline in AD patients: Eldholm, RS et al, J. Alz. Disease, 61: 1221, 2018. Suh, GH et al., Intl. J. Geriatric Psychiatry, 19(9): 817, 2004.

# Corporate Overview



# Financial Snapshot - Nasdaq: CYTH

Cash  
Balance<sup>1</sup>

\$19.3

Market  
Cap<sup>2</sup>

~\$28M

Shares  
Outstanding

8.4M

Average  
Volume<sup>2</sup>

~101K

1: Pro-forma at 9/30: Included proceeds from public offering on 11/17/2021

2: As of March 1, 2022 with a closing price of \$3.29

# Investment Summary

Leveraging over 3 decades of experience with cyclodextrins to advance clinically de-risked programs towards approval in diseases with unmet medical need

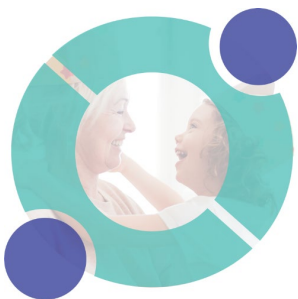
Platform technology has demonstrated to be safe and effective with over 10 years of patient exposure

## TransportNPC™

Global site activation ongoing and currently enrolling patients in Pivotal Phase 3 study in Niemann-Pick Disease Type C

Received IND Clearance to Advance Phase 2 Study in Alzheimer's Disease

Well funded through key value-driving clinical and regulatory milestones  
Trappsol® Cyclo™ is a platform technology with opportunity to expand into multiple indications  
Leadership team with proven track-record in execution and value creation



NASDAQ: CYTH  
cyclotherapeutics.com

cyclo  
therapeutics

The logo for cyclotherapeutics features the word "cyclo" in a large, teal, sans-serif font. The letter "o" is stylized with two dark blue circles on its right side. Below "cyclo" is the word "therapeutics" in a smaller, dark blue, sans-serif font.

*Thank you!*