



# cyclo therapeutics

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# Investment Opportunity

Deep expertise with Cyclodextrins with over 10 years of patient exposure

Lead program, Trappsol<sup>®</sup> Cyclo<sup>™</sup> demonstrated to be safe and effective in multiple clinical studies in NPC

Significant market opportunity in high value indications

Leadership team with proven expertise

Manufacturing at commercial scale inclusive of 60-month stability and 96hr In-use stability

## Currently Targeting 2 Serious Diseases with Unmet Medical Need

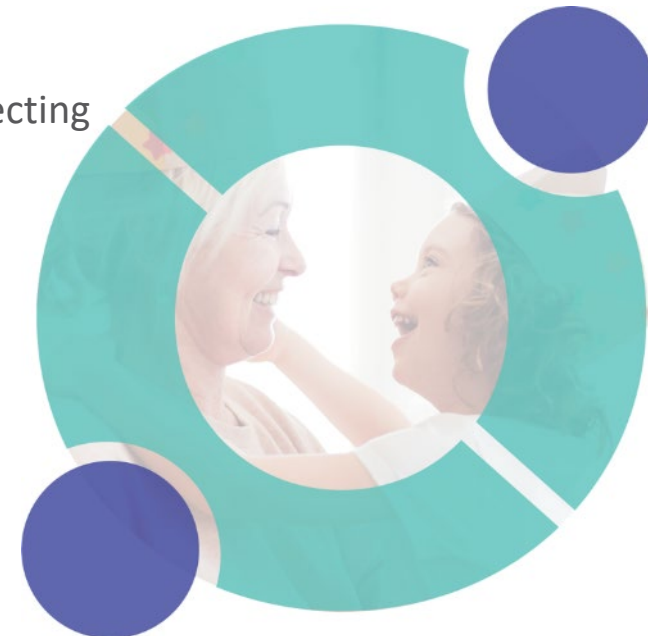
### Niemann Pick Disease Type C

Fatal and progressive genetic disorder  
Orphan indication affecting >9,000 in 80 countries (~400 in U.S. / 320 EU5)<sup>1</sup>

### Alzheimer's Disease

6<sup>th</sup> leading cause of death affecting 5 million people in the U.S.<sup>2</sup>

Platform technology has potential to fuel pipeline expansion opportunities



1. April 2021, 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 in United States + 79 other countries.  
2. <https://www.alz.org/alzheimers-dementia/facts-figures>

# Pipeline



# Leadership Team with Proven Experience



**N. Scott Fine**  
Chief Executive Officer & Director



**Joshua M. Fine**  
Chief Financial Officer



**Gerald F. Cox, M.D., Ph.D.**  
Acting Chief Medical Officer



**Michael Lisjak**  
Chief Regulatory Officer



**Sharon H. Hrynkow, Ph.D.**  
Chief Scientific Officer



**Russ Belden**  
Acting Chief Commercial Officer



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



**Lori McKenna Gorski**  
Global Head of Patient Advocacy



# Niemann-Pick Disease Type C

Site activation ongoing and currently enrolling patients in the Pivotal Phase 3 study, TransportNPC™

The TransportNPC™ trial is currently the most advanced clinical research program underway to identify a treatment for NPC.



# Niemann-Pick Disease Type C (NPC)

Rare, fatal and progressive genetic disorder characterized by a defect in the NPC1 protein causing cholesterol and lipids to accumulate in cells of major organs leading to cell and tissue dysfunction.

## Average Life Expectancy:

Before age 5 if symptoms appear in infancy

Age 20 in juvenile onset





Increasing diagnosis in later onset disease

## Symptomology Inclusive of Systemic and Neurological Manifestations

- Enlarged liver and spleen (hepatosplenomegaly)
- Severe liver disease and dysfunction
- Respiratory infections and lung disease
- Loss of cognitive skills
- Difficulty with speech
- Seizures
- Difficulty with swallowing and feeding
- Difficulty coordinating movement (ataxia)
- Abnormal eye movements (vertical supranuclear gaze palsy)
- Poor muscle tone (hypotonia)

No U.S. Approved NPC Therapies  
Only 1 E.U. Approved Therapy

# Significant Competitive Advantages

Company	Product / Route	Descriptor	Potential Indication
	Trappsol® Cyclo™ (Intravenous every 2 weeks)	Met all primary endpoints of the Phase 1 and Phase 1/2 studies showing favorable safety and efficacy. Site activation ongoing and currently enrolling patients in Pivotal Phase 3 study, TransportNPC™.	Systemic and Neurological
	Zavesca* (Oral 3 times daily)	EU and other international countries approved. Off-label in the US.	Neurological
	Arimoclomol (Oral 3 times daily)	FDA provided a Complete Response Letter 17-Jun-2021 citing additional qualitative and quantitative evidence was needed to show the drug's effectiveness.  EMA submission completed November 2020, expected feedback H2 2021, with potential approval Q1 2022.	Neurological
	IB1001 (Oral 3 times daily)	Met with FDA, EMA and UK to discuss Phase 2 results. 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.	Neurological

\*Only approved Treatment (non-US)

# NPC Prevalence

## Incidences

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

## Existing Cases

>9,000 in 80 countries  
(~400 in U.S. / 320 EU5)

## Of Diagnosed Patients

~ 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

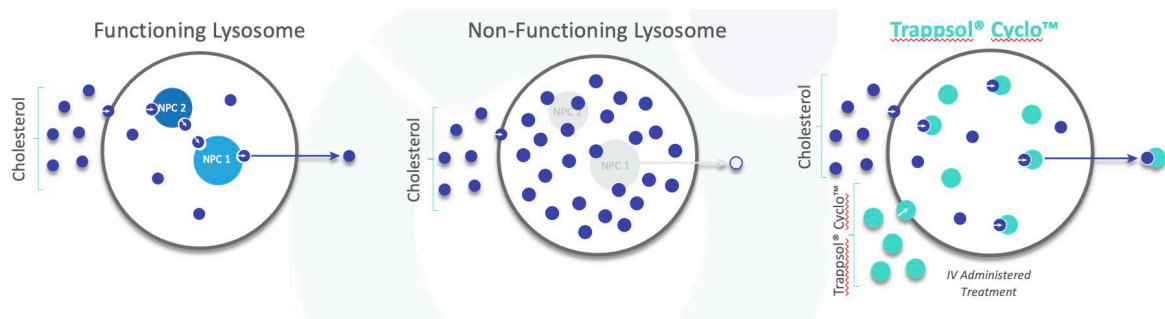
\*Scope: United States + 79 other countries; \*Commissioned Tessellon Inc – former Kantar Health experts with 25+ years of epidemiology and forecasting experience, ([www.Tessellon.com](http://www.Tessellon.com)); \*Exhaustive literature search with a broad range of MESH terms.

# Cyclo Therapeutics Scientific Rationale for NPC

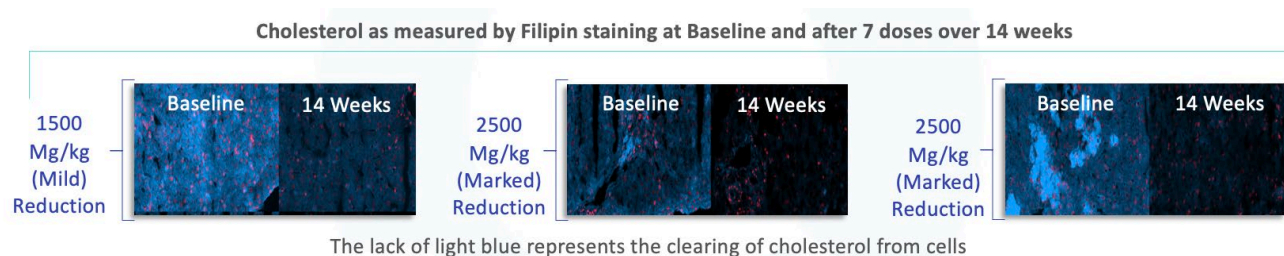
## Mechanistic attributes of Trappsol® Cyclo™

- Trappsol® Cyclo™ is a hydroxypropyl-beta-cyclodextrins (HPBCDs) and has an affinity for cholesterol. What distinguishes the clinical program is the Intravenous Route of Administration allowing the drug to reach major peripheral organs and shown in studies to clear cholesterol from cells peripherally...

**Figure 1: Mechanism of Action**



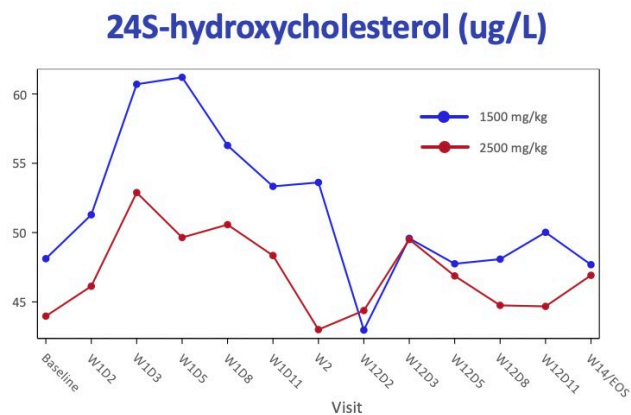
**Figure 2: Cholesterol Clearance from Liver cells**



- and centrally, affects CNS biomarkers and underpin neurologic outcomes as demonstrated in our current data from our completed and ongoing studies.

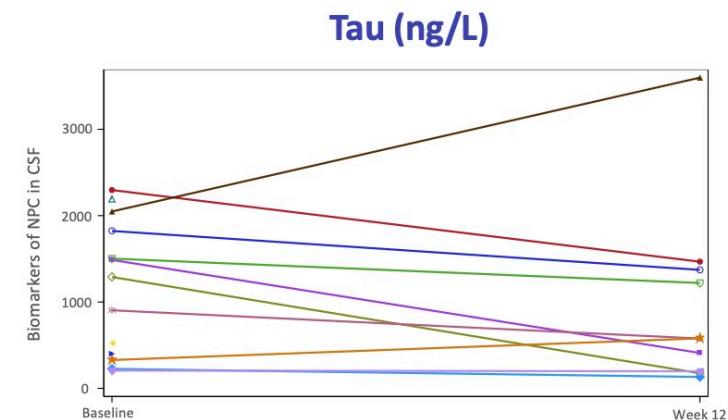
**Figure 3: Reduction in Brain Cholesterol**

**24S-hydroxycholesterol**, a cholesterol metabolite from the CNS transported across the BBB, increases in serum following IV administration of HPβCD. Shown here are data after 1<sup>st</sup> dosing and 7<sup>th</sup> dosing. 24S-hydroxycholesterol increases in serum following IV infusion of HPβCD, signaling removal of excess cholesterol from the brain.



**Figure 4: Reduction in Tau**

**Tau** levels as measured in the CSF are shown here for 10 NPC patients who had lumbar punctures prior to treatment with HPβCD and after seven doses. **Six of 10 patients** showed a reduction in Tau levels, two remained stable, and two increased, no dose-response relationship.



# Trappsol® Cyclo™

## Development Path Towards Potential Approval

### Phase 1

Completed May 2020

- ✓ Favorable safety and tolerability profile
- ✓ Removal of trapped cholesterol
  - ✓ Drug present in CSF
- ✓ Increase in 24S biomarker
  - ✓ Decrease in Tau

### Phase 1/2

Encouraging Topline Results  
Reported March 2021

- ✓ Favorable safety and tolerability profile
- ✓ 100% of patients who completed the trial improved or remained stable per their treating physicians
- ✓ Demonstrated improvements in ataxia, swallow, walking and Quality of Life

### TransportNPC<sup>®</sup> (Pivotal Phase 3)

Site activation ongoing and currently enrolling patients

- ✓ Global clinical protocol agreed with U.S. FDA and EMA
- ✓ EMA PDCO agreed to Sub-study in patients 0-3 years of age in EU only
- ✓ EMA PDCO feedback stated it has potential as a preventative

Orphan Drug Designation in U.S. | Fast Track Status in U.S. | Potential for Priority Review Voucher (PRV) in U.S

Rare Pediatric Disease Designation | Orphan Designation in EU | EMA Pediatric Investigational Plan Adopted

# Applying Development Insights to Ph3 Program

## Clinical Attributes for Trappsol® Cyclo™

- Has a favorable safety profile, no permanent hearing losses associated, high patient acceptability and is able to be used in a Home setting

## Data represented:

- The data presented are from Topline results from our 201 study and a data cut from September 2020 from our 102 study. This data has not been formally QC'd.
  - A Zero (0) or Negative number represents stabilization or improvement

## Summary for applying to Ph3 Study:

- Primary Endpoint is the mean change from baseline to 48wks or 96wks as measured by improvement in the NPC-SS of Trappsol® Cyclo™ over Placebo
- Designed with FDA and EMA feedback to deliver higher probability of clinical and regulatory success:
  - Increased number of Patients for increased power of study
  - Included ASIS scoring within inclusion criteria to have a more accurate view of patient trajectory
  - Increased Study duration to 2-years with a 1-year Interim Analysis to capture disease progression
  - Finalized Primary Endpoints with 4D-NPC-SS (AM, FM, SP and SW) for United States and 5D-NPC-SS (AM, FM, SP, SW and CO) for Non-US.

Based on natural history data with no intervention, patients would be expected to decline on average by +1.5 points per year.

Dose	Age	Study	Patient ID	17D-NPC-SS (201 Primary was -1pt reduction in ≥ 2 Domains)	Change Total Score (17D)	Change Total Score (5D)
1,500	15	201	301-02	Withdrawn before wk 12	-	-
1,500	34	201	001-01	Withdrawn after wk24	6	5
1,500	6	201	302-02*	Withdrawn after wk36	8	4
2,000	39	201	201-01	Week 48 (EM-1, FM-1,D7-1)	-3	-1
1,500	2	201	301-04	Week 48 (AM-3,FM-1)	-2	-3
1,500	4	201	003-03	Week 48 (MM-1,D1-1,D6-1)	-2	0
2,000	11	201	301-03*	Week 48 (AM-1,SW-2,D1-2,D2-1,D3-1,D4-1,D5-1)	-4	0
2,000	2	201	301-05	Week 48 (EM-1,CO-2)	-1	-1
2,000	2	201	003-02	Week 48 (FM+1,CO+2,D2+1)	4	3
2,500	21	201	001-02	Week 48 ( SW-1,SZ-2,D1-1,D4-1)	-3	1
2,500	3	201	302-01	Week 48 (EM-1,SP-1)	1	0
2,500	8	201	003-01*	Week 48 (D1-1,D4-1)	3	2
1,500	37	102	001-01	10 months	0	0
1,500	30	102	001-02*	10 months	0	-1
1,500	69	102	001-07*	7 months	0	0
1,500	64	102	001-08*	6 months	0	0
1,500	20	102	001-09*	8 months	-3	0
1,500	60	102	001-11*	8 months	-2	0
2,500	21	102	001-04*	10 months	-3	0
2,500	18	102	001-10*	5 months	-2	0
<b>Mean Change: All patients for 201 = 11</b>					<b>0.64</b>	<b>0.91</b>
<b>Mean Change: All patients for 201 (11) and enrolled 102 (8) = 19</b>					<b>-0.16</b>	<b>0.47</b>
<b>Mean Change: Patients who completed 201 = 9</b>					<b>-0.78</b>	<b>0.11</b>
<b>Mean Change: Patients who completed 201 (9) and enrolled in 102 (8) = 17</b>					<b>-1.00</b>	<b>0.0</b>
<b>Mean Change: Patients not on miglustat who completed 201 (2) and enrolled in 102 (7) = 9</b>					<b>-1.22</b>	<b>0.11</b>
<b>Percentage of all patients who have Improved or Stabilized from total of 19</b>					<b>74%</b>	<b>74%</b>

\* No Miglustat

AM, ambulation; FM, fine motor; SP, speech; SW, swallow; CO, cognition; EM, saccadic eye movement; MM, memory; SZ, seizure management  
D = modifier domains, including cataplexy, narcolepsy, behavioral issues, respiratory, incontinence.

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

# Patient Progress: A Case Study

## 61-year-old patient with NPC: Improvements with intravenous (IV) Trappsol® Cyclo™ over 15 months

Diagnosed at age 59 years: slurred speech, ataxia, vertical gaze palsy, mild dysmetria/dystonia, mild hearing loss, mild short term memory loss with intact cognition, cough with eating

Completed Phase 1 trial and received 7 infusions IV Trappsol® Cyclo™; no toxicities

Currently enrolled on extension protocol and receives IV Trappsol® Cyclo™, 1500 mg/kg every 2 weeks at home

Patient and spouse see notable improvements in speech and swallow, seen within hours of the infusion and maintained for 5-10 days

- Increased speech fluency and word finding, more comfortable to communicate, more interactive and happy, positive impact on quality of life
- Takes solids and un-thickened liquids without cough; rare cough on saliva every few weeks
- Clinical severity score improved by 1 point due to change in cough; scale for speech does not include changes in speech fluency/word finding
- Cognition remains stable



# Alzheimer's Disease

Filing IND in H2 2021 for  
potential 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>

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

FDA feedback from Type B meeting supports Phase 2 development strategy  
for Alzheimer's Disease asset; IND filing on track for H2 2021

## Positive Results in Alzheimer Patient Under Compassionate Use Program

FDA authorized use of Trappsol® Cyclo™  
in geriatric patient

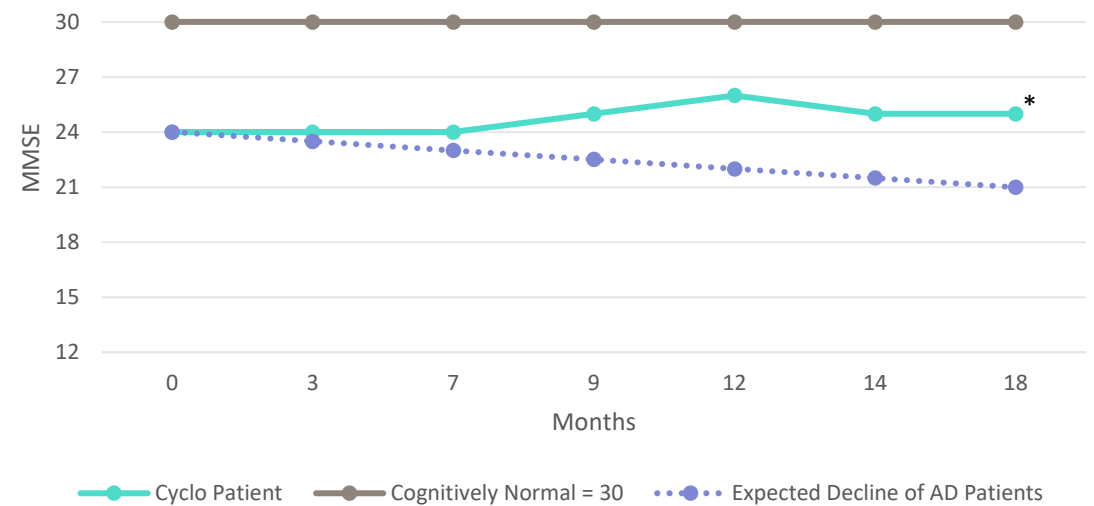
18 months of monthly IV infusion

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

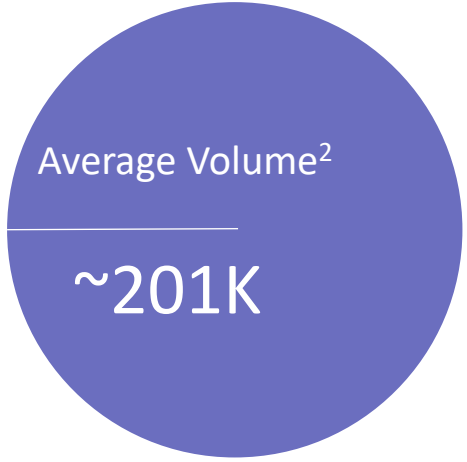
\*Treating physician reported the 18-month score as a range between 24-26

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

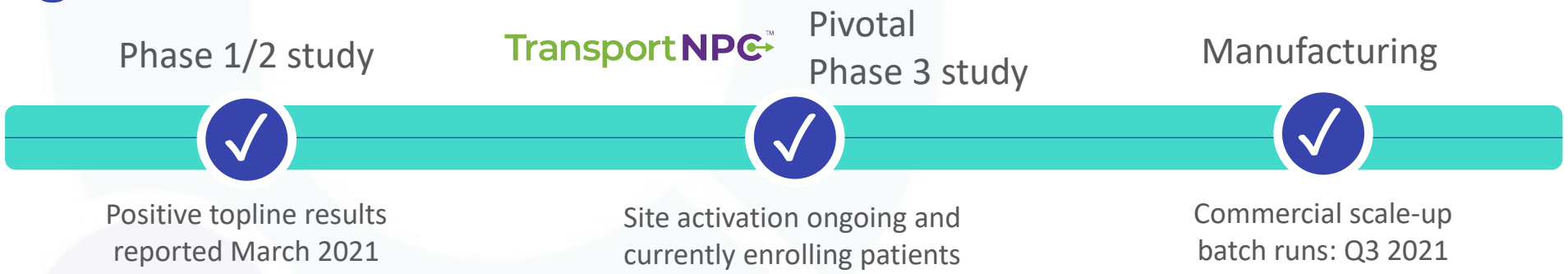


# Financial and Capital Markets Snapshot

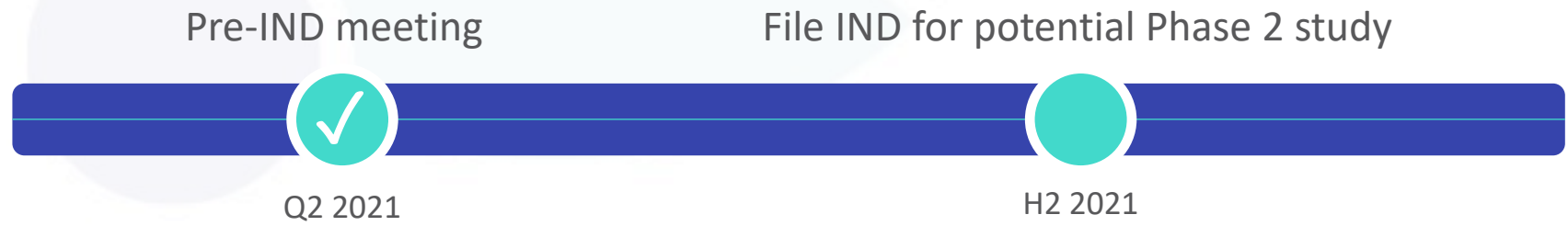


## Target Upcoming Milestones with Potential to Drive Value

Niemann-Pick Disease Type C



Alzheimer's Disease



# Investment Summary

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

## TransportNPC™

Lead asset demonstrated to be safe and effective with over 10 years of patient exposure

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

Significant market opportunity with no approved therapy to treat both systemic and neurological manifestations of NPC

Planning and executing pre-approval commercialization imperatives

Pipeline expansion into Alzheimer's Disease (AD), patent pending

AD IND filing on track for H2 2021



Multiple value-driving milestones expected throughout 2021

Platform technology with opportunity to expand into multiple indications

Leadership team with proven track-record in execution and value creation

# Board of Directors



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Chairman

President & CEO of Polpharma Group  
Independent Director



F. Patrick Ostronic

Vice Chairman

Officer of US Pharmacia International & CFO of The USP Group  
Independent Director



N. Scott Fine

Chief Executive Officer & Executive Director



Jeffrey L. Tate, Ph.D.

Chief Operating Officer, Chief Quality Officer & Executive Director



C.E. "Rick" Strattan

Founder, Former Director of Marketing & Business Development of Pharmatec  
Independent Director



William S. Shanahan

Former President & COO of Colgate-Palmolive  
Independent Director



Randall M. Toig, M.D.

Associate Professor at Northwestern University, Northwestern Memorial Hospital  
OBGYN Surgeon & Serial Entrepreneur  
Independent Director



# 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.



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.



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.



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.



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*Thank you!*

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