Cyclo Therapeutics Is Entering the Race to Find a Treatment for Alzheimer's Disease

Up until very recently, Cyclo Therapeutics which is a microcap biotech company with a tiny float (6.4M shares outstanding) was the leading company in the race to find a treatment for NPC. NPC is a rare form of dementia that is often referred to as Children's Alzheimer's.

Company is looking to submit an IND application before the end of this year to enter Trappsol Cyclo, which is a proprietary formulation of hydroxypropyl beta cyclodextrin, in Phase 2B of Alzheimer's clinical trials. Company will skip Phase 1 of Alzheimer's clinical trials as Trappsol Cyclo has already shown safety profile in NPC clinical trials (currently enrolling patients for NPC for Phase 3 of the clinical trials).

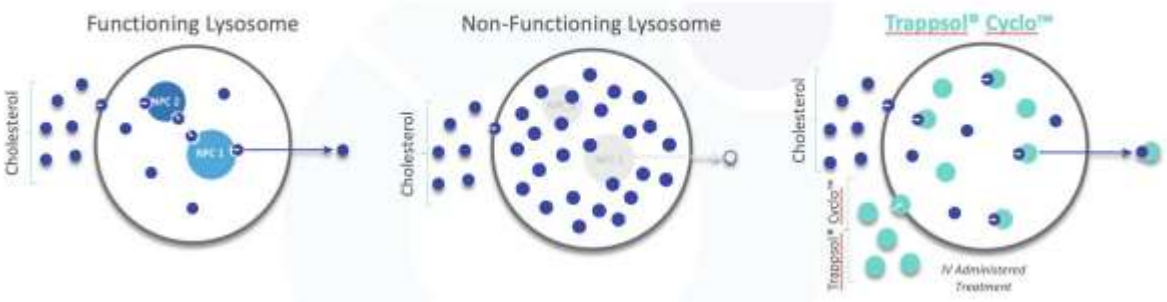
Company is looking to expand its pipeline to Alzheimer's on the basis of the findings from its NPC clinical trials, strong mouse models of AD, and a single patient expanded access Alzheimer's clinical trial that saw no signs of progression of the disease in the patient for 18 months.

How Does Trappsol Cyclo work?

Trappsol Cyclo which is a proprietary formulation of hydroxypropyl beta cyclodextrin, is a donut shaped molecule that is administered intravenously and has an affinity for cholesterol.

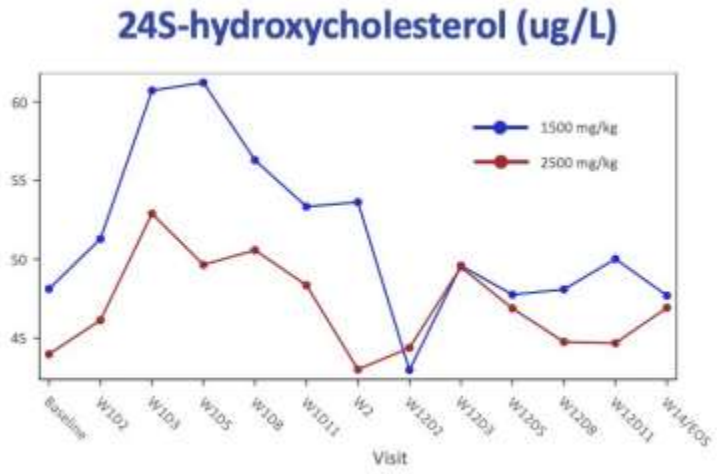
Below is a chart from company's investor presentation deck that shows the mechanism of action of Trappsol Cyclo. As can be seen below, in patients that lack NPC1 protein, cholesterol gets stuck in cells and this eventually leads to choking and death of cells. When patients are treated with the drug, trapped cholesterol gets stuck in Trappsol molecules and these donut shaped molecules help remove excess cholesterol from cells.

Figure 1: Mechanism of Action

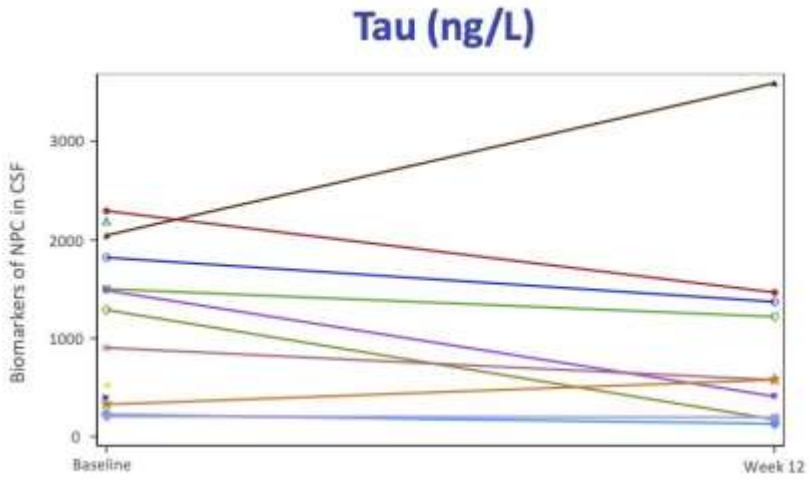


Trappsol Cyclo has also shown to have an impact on CSN biomarkers. Despite its large size, this elegant molecule, manages to cross the blood–brain barrier and amongst other things, impacts the cholesterol level in the brain as well as tau levels.

Below is a chart from the company's NPC clinical trials which shows how 24S-hydroxycholesterol, a cholesterol metabolite from the CSN transported across the BBB, increases in Serum following IV administration of Trappsol Cyclo. 24S-hydroxycholesterol increases in serum following IV infusion of Trappsol Cyclo, shows removal of excess cholesterol from the brain.



Trappsol Cyclo infusion also leads to reduction in Tau in the brain. 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.



Why I believe Cyclo Therapeutics is going to be relevant treatment of Alzheimer's disease:

Reason #1: Linkage between Cholesterol and Alzheimer's:

In August 2021, in a study that was published by scientists from the University Of Virginia School Of Medicine a team co-led by scientists at Scripps Research used advanced imaging methods that showed how the production of the Alzheimer's-associated protein amyloid beta (Aβ) in the brain is regulated by cholesterol.

The scientists' work helped us better understand how Alzheimer's disease develops and underscores the long ignored role of brain cholesterol. This study also helped explain why past studies have linked Alzheimer's risk to a cholesterol-transporting protein called apolipoprotein E (apoE).

"We showed that cholesterol is acting essentially as a signal in neurons that determines how much Aβ gets made-; and thus it should be unsurprising that apoE, which carries the cholesterol to neurons, influences Alzheimer's risk." noted Scott Hansen, PhD, study co-senior author, associate professor, Department of Molecular Medicine at Scripps Research, Florida.

For those of you unfamiliar with the history and roots of Alzheimer's disease, excess Aβ in the brain can create clumps that are referred to as plaques and these plaques can choke up and kill neurons in the brain, and the eventual death of these neurons have been linked as the main cause of Alzheimer's disease. Brain needs healthy neurons to form new experiences and make connections to the past experiences that are known as memories.

Cholesterol's role in Alzheimer's disease had been suggested by various prior studies but never confirmed directly, due to technological limitations. The scientists at University Of Virginia School Of Medicine used an advanced microscopy technique called super-resolution imaging to "see," in cells and in the brains of live mice and tracked how cholesterol regulates Aβ production.

As I had noted previously in this paper, Cyclo Therapeutics has shown that its drug can cross the BBB and it can remove excess cholesterol (that has now been linked with the creation of excess Aβ) from the brain. This direct relationship is the first glaring evidence that Trappsol Cyclo could work on slowing down the progression of Alzheimer's disease or even stopping it.

Reason #2: Linkage between Alzheimer's and Tau levels

Tau which is a protein that is predominantly found in brain plays an important part in normal functioning of the brain. In a healthy brain, neurons are supported internally by structures called microtubules, which help guide nutrients and molecules from the cell body to the axon and dendrites. In healthy neurons, tau normally binds to and stabilizes microtubules. In Alzheimer's disease, however, abnormal chemical changes cause tau to detach from microtubules and stick to other tau molecules, forming threads that eventually join to form tangles inside neurons. These tangles block the neuron's transport system and blocks communication between neurons.
Reducing the amount of misfolded tau in the brain is therefore, one of the ways scientists have tried to target in attacking Alzheimer's.

As noted previously, and based on company's NPC trial results, Trappsol Cyclo has shown ability to reduce or stabilize tau levels in the brain.

Reason #3: Mouse Models and Expanded Access study

In a study that was published back in 2012, scientists showed that hydroxypropyl-β-CD (Trappsol Cyclo is a HP-β-CD formulation) HP-β-CD:

- reduced cell membrane cholesterol and amyloid-β production in a cell model
- improved learning and memory in mice
- significantly reduced Aβ plaque load and microgliosis
- decreased Aβ production and amyloidogenic processing
- reduced tau pathology
- corrected lysosomal abnormalities
- up-regulated genes involved in cholesterol trafficking

Granted that mouse models cannot be relied on heavily when it comes to neurodegenerative diseases, the outcomes from this mouse study cannot be ignored.

Based on the above mouse model and back in 2018, a family office approached the company and requested the company's drug to be used on a single patient. Company requested and FDA authorized use of Trappsol Cyclo in this geriatric patient.
For 18 months this patient was treated with Trappsol Cyclo and Alzheimer's disease did not progress in this patient.

"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", noted the Principal Investigator at the end of the study.

Current valuation of the company:

Company has a float of 6.44M shares outstanding. At current share price of $7.07, market is valuing this company at $45M.

Below is my valuation model for the company. This valuation model completely ignores the Alzheimer's asset potential for this company:

Total Addressable Market	$ 150,000,000	Conservative figure (Actual number is somewhere between $150M to $500M
Assumed Market Share	50%	(Again a super conservative figure. CYTH is the leading company in NPC race)
Profit Margin	90%	(per compassionate use of the drug and past financial statements)
Annual EBITDA	67,500,000	
Success probablity of approval	30%	Per https://www.toptal.com/finance/valuation/biotech-valuation , actual probability of approval is 59%, I took a conservative 30% figure
Risk adjusted EBITDA	20,250,000	
EBITDA Multiple	10	Company will actually have 12 years of exclusive sale of the drug
Prevent Value of Annuity (FMV of company today)	156,365,132	
Fair Share Price today based on the above valuation model, which ignores drug's potential in treating Alzheimer's disease		
Fair Market Cap per above	156,365,132	
Total number of shares outstanding	6,440,000	
Fair Share Price Today **	**$ 24.28**	
** Above share price COMPLETELY disregards the Alzheimer's potential and its impact on company's Market Cap and share price		
*** Above calculation is PURELY my personal (MarketWatchTrends) Valuation Model for valuing Cyclo Therapeutics and should not be relied on by others		

It is clear from the above valuation model that market is not even properly putting a fair value on this company for its NPC asset.

Add to the above, the fact that company is looking to make an IND Application (before the end of 2021) to enter the Alzheimer's race and if FDA approves the IND Application (FDA will respond to the IND application within 30 days), company will kickstart Phase 2B of the clinical trials for Alzheimer's disease.

Comparing this company's potential pipeline a few weeks from today, with other companies, and given how some of those companies could be considered far behind Cyclo Therapeutics in their clinical trials,

but have far larger market capitalizations, one could say, Cyclo Therapeutics is being severely undervalued by the market right now. Especially given the reasons I provided to you above as to why Cyclo Therapeutics could be more relevant in the Alzheimer's race than most realize.

Company's Current Cash Balance:

Company is currently sitting on anywhere between $8M-$10M of cash (estimated amount). Company has a $20M ATM ready to be used if/when company sees fit (most likely will use ATM when IND Application is made).

Conclusion:

Cyclo Therapeutics is the leading company in the race to find a treatment for NPC which is a rare form of dementia. However, this company is potentially sitting on an asset that could potentially be a disease altering treatment for the common form of dementia.

Given how market has put such a low valuation on this company (basically ignoring any value that Alzheimer's could potentially bring this company and how market doesn't even properly value its NPC potential), I see unmatched risk/reward level for this company at these current valuations.