Licensing / Collaboration Opportunity

ASDERA

Advanced Statistics for Drug Exploration, Reformulation & Approval

Summary:

ASDERA is proposing an exclusive / non-exclusive license or collaboration on new treatments for Alzheimer's/Parkinson's/Huntington/s disease (AD/PD/HD), MS and ALS, with first trials ready for NDA within 2.5 years.

Field:

A pharmaceutical intervention comprising novel derivatives ASD-005 of Hydroxypropyl-α-cyclodextrin (HPαCD) for the treatment of neurodegenerative diseases (ND).

US Market (at $20,000/yr/pp)

10% of 5.5M↗ AD = US $11.0B/yr

10% of 1.0M↗ PD = US $ 2.0B/yr

10% of 0.5M↗ MS = US $ 1.0B/yr

HD/ALS: orphan diseases

Patent status

Internat. composition-of-matter (CoM) patent applications PCT/US2018/051604
Priority date: March 20, 2016.
Inventor: Knut M. Wittkowski,
Assignee: ASDERA LLC

Development status

505(b)(2): IND/ODD-ready at $500K each for preparation for 2b/3 trials. The first clinical studies are planned in HD, ALS, GBA-PD, and PP-MS.

Relevant Publication

Wittkowski KM, Dadurian C, Kim HS, Hoshino A, Lyden D. (2018). (Wittkowski 2018) http://www.doi.org/10.1371/journal.pone.0199012

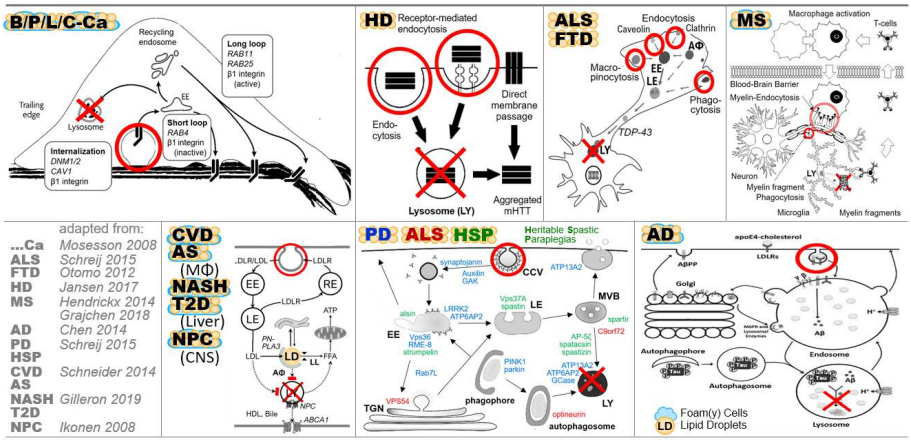
A Lipid-Carrier Nano-Device Against Progression in Neurodegenerative Diseases (ND)

Background / Unmet Need

ND affect >7M US people, yet no disease-modifying treatments are available. Many of the PD patients develop dyskinesias and the effects of symptomatic treatments "wear off". GBA-associated PD often manifests at younger age and causes more significant cognitive impairment. Primary progressive (PP) MS also affects younger people.

Description of the Invention

A common component in the etiology of NDs (and cancers)(Devine 2011) is "deranged" (AD), "defective" (PD), "derailed" (cancer), "dysregulated (ALS)" **(Mosesson 2008; Otomo 2012; De Franceschi 2015)** endocytosis, one of the few biologic processes that do not decline with age. The invention aims to down-regulate serum phospholipids (PL) by HPαCDs to prevent aging cells from being overloaded and accumulating Aβ/tau (AD), α-syn (PD), and myelin (MS), mHTT (HD), and SOD1 (ALS).



Proof of Concept

βCDs have been effective *in vivo* against cancers,(Grosse 1998; Zhang 2006) AD,(Yao 2012) and PD.(Bar-On 2006; Li 2015). HPαCD is more effective against breast cancer than HPβCD (Wittkowski 2018) (see below for *in vivo* results).

Applications

Oral (or intrathecal) ASD-005 is effective against neurodegenerative diseases, including AD, (GBA-)PD, HD, ALS, and MS.

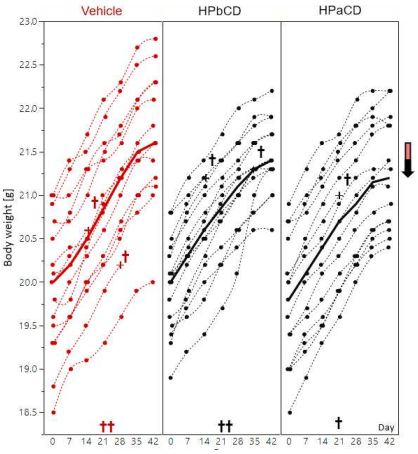
Competitive advantages

- Many PD patients inevitably become refractory to L-dopa.
- Treatment options for AD, HD, MS, and ALS are limited.
- HPβCD is in Ph 2 against NPC disease, but was abandoned in ND due to the risk of permanent hearing loss (not applicable to αCDs).
- αCD (in the US) and αCDs (in the EU), are recognized as safe for oral (US: GRAS) and parenteral use (EU, US: Caverject®).

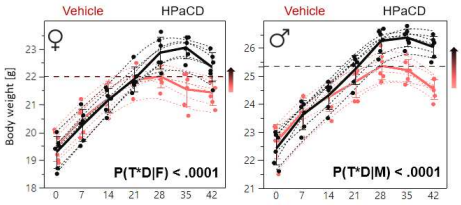
EEC and LY Function Across Diseases and Conditions

In vivo studies in mouse models of monogenic forms of HD and ALS

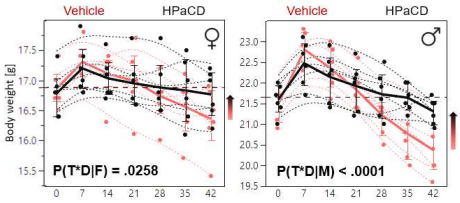
Control: HPαCD reduces **weight gain** in NGS mice



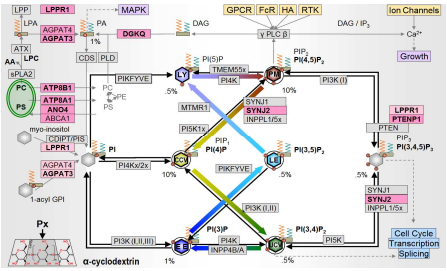
HPαCD reduces **weight loss** in SOD1 (**ALS**) mice



HPαCD reduces **weight loss** in HTT (**HD**) mice



***GWAS*: Influx of PC into the PI-cycle drives endocytosis (GWAS).**



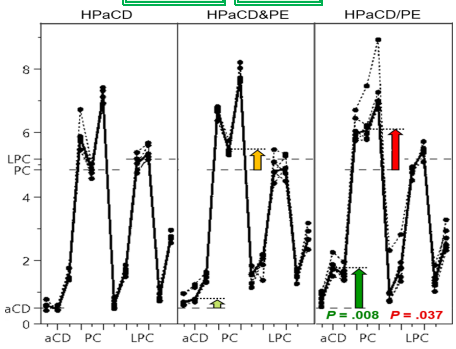
Pink: Genes significant in BCa GWAS.

***In vitro*: HPαCD is 2× as effective as the ototoxic HPβCD against migration of HR⁺ and TN BCa cells.** (Wittkowski 2018)

***In vivo*: αCD was effective in a NPC model.** (Davidson 2016) **HPαCD is more effective than was HPβCD** (Grosse 1998) **against tumor growth, metastases, and inflammation in a BCa model (NGS),** (see PCT)

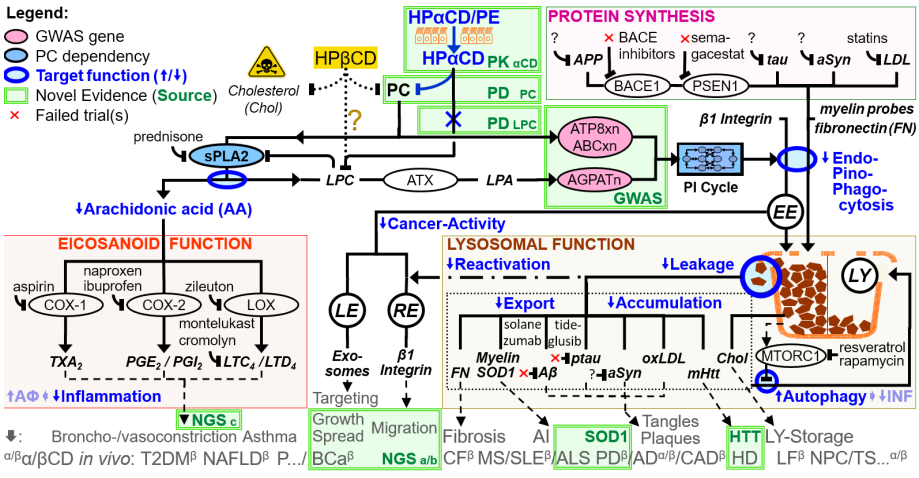
HPαCD also reduces disease-specific weight loss in models of HD (HTT) and ALS (SOD1). (above)

Human PK αCD/PD PC



FPLC of morning urine. HPαCD is not absorbed; ASD-005, the HPαCD"/"PE (penetration enhancer) compound is absorbed better (⬆) than the mixture ("&", ⬆). PC is excreted proportionately (⬆/⬆), but lyso-PC (LPC) is not, avoiding compensatory activation of (sPLA2), resulting in ↓Inflammation via ↓AA in addition to ↑AΦ via ↓Endo-/Pino-/Phagocytosis (PI cycle).

ASD-005 Reduces Inflammation and Improves Autophagy



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