MELIOR PHARMACEUTICALS®

Mesocarb

A novel clinical stage drug candidate to treat Parkinson's Disease Levodopa-Induced Dyskinesia (PD-LID)

- New highly selective and well tolerated dopamine reuptake inhibitor with significant benefits over older drugs:
  - *Well known clinical safety profile; previously marketed outside US for various CNS conditions*
  - *Robust attenuation of levodopa induced dyskinesia*
  - *Potentiates anti-Parkinsonian activity of levodopa*
  - *Stabilizes disrupted sleep-wake cycle associated with PD*
  - *Efficacy and safety comparable to, or better than, amantadine*
- Rigorous exclusivity strategy based on issued patents
- Phase 2-ready, with potential to initiate US registration studies within 18-24 months

Overview

Melior Pharmaceuticals Inc. is developing mesocarb, a therapeutic candidate for Parkinson's disease levodopa-induced dyskinesia, a debilitating side effect of levodopa therapy[Note1]. PD-LID is estimated to develop in over 90% of patients who have been on levodopa treatment for over five years. This represents up to 200,000 patients in the US.

The effects of PD-LID can be as debilitating as the primary effects of the underlying Parkinson's disease. Dyskinesia can reduce independence, activities of daily living and quality of life significantly. Unfortunately, PD patients often adopt levodopa sparing treatment regimens to avoid worsening of PD-LID, leading to sub-optimal management of their Parkinson's disease. Amantadine is the only currently available treatment option for PD-LID. However, it is associated with high CNS and GI side effects.

Mesocarb is the most selective dopamine reuptake inhibitor (DRI) to be characterized. Melior has discovered that this selectivity is critical in differentiating mesocarb from other, less selective DRIs, in the context of PD. This unique activity profile of mesocarb provides for 1) therapeutic benefit towards PD-LID, 2) potentiation of levodopa therapeutic effects and 3) stabilized disrupted sleep-wake cycle associated with PD[Note 2]. In addition, this therapeutic benefit is accompanied by exceptional safety and tolerability as demonstrated by over 1 million patient-years exposure.[Note 3]

Melior plans to initiate a Phase 2b proof of efficacy study in PD-LID subjects in early 2019.

Background

Mesocarb has already demonstrated clinical efficacy, safety and tolerability from its marketing experience outside the US in a variety of CNS indications.

- Over one million patient years exposure
- Over 40 clinical publications

Melior is now developing mesocarb in Parkinson's disease levodopa induced dyskinesia, given compelling preclinical data in animal models of PD-LID:

- Reduces levodopa induced dyskinesia in parkonsonian rats
- Highly targeted approach; strong in vivo affinity and selectivity for DAT
- Enhances anti-parkionsonian activity of levodopa activity
- Promotes wakefulness without sleep rebound
- Superior tolerability than amandatine

Partnering Thesis

Melior is seeking investors to support clinical development of mesocarb in PD-LID. Melior plans to initiate a Phase 2b PD-LID study in 1H 2019. A successful Phase 2b study will advance mesocarb to US registration studies within 24 months, positioning mesocarb as one of the only clinical stage candidates in development for PD-LID specifically and Parkinson's disease in general.

Team and Track Record

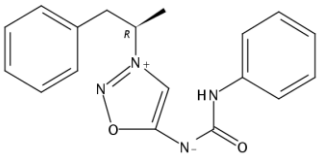
Melior Pharmaceuticals is a mid-staged biopharmaceutical company developing a pipeline of de-risked, molecules in therapeutic areas of significant unmet need. Our management team has had a track record of success identifying and developing de-risked drug targets that have potential for accelerated clinical development in therapeutic areas with significant unmet needs. [Note 4]

For Further Information Please Contact:

Mahen Gundecha, Chief Business Officer
Email: mgundecha@meliorpharma.com
Tel. 484-354-4274

Notes

1. MLR-1019 nomenclature

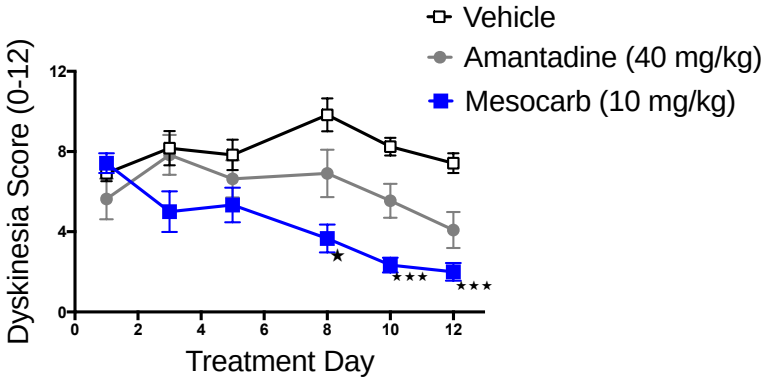


Mesocarb has one chiral center meaning that the compound can be separated into 2 stereoisomers. One of these isomers is biologically active and the other stereoisomer is relatively biologically inactive by all perspectives for which Melior and others have evaluated it. For our purposes and reference to the studies herein mesocarb may refer either the racemic form orthe isolated active enantiomer.

2. Brief summary of Melior's data illustrating PD therapeutic benefit

Melior has conducted numerous studies of mesocarb's activity in rodent models of Parkinson's disease including the unilaterally 6-OHDA-lesioned rat model, generating hemiparkinsonian rats.

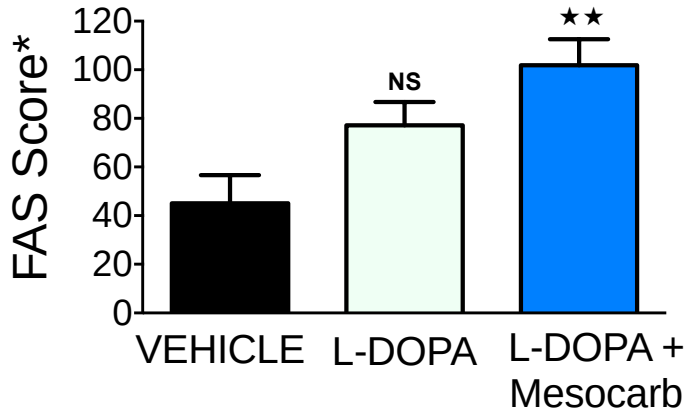
Mesocarb reduces dyskinesia score in hemiparkinsonian rats after chronic administration as compared to amantadine



Hemiparkinsonian rats were primed with levodopa to induce abnormal involuntary movements (AIMS) (a form of dyskinesia). Animals were treated with vehicle, mesocarb or amantadine and scored for dyskinesia. Data are significantly different from the vehicle treated animals, P<0.05, P<0.001. Additional studies reveal the benefit of the active enantiomer versus the racemic form

Mesocarb Improves the Therapeutic Activity of levodopa

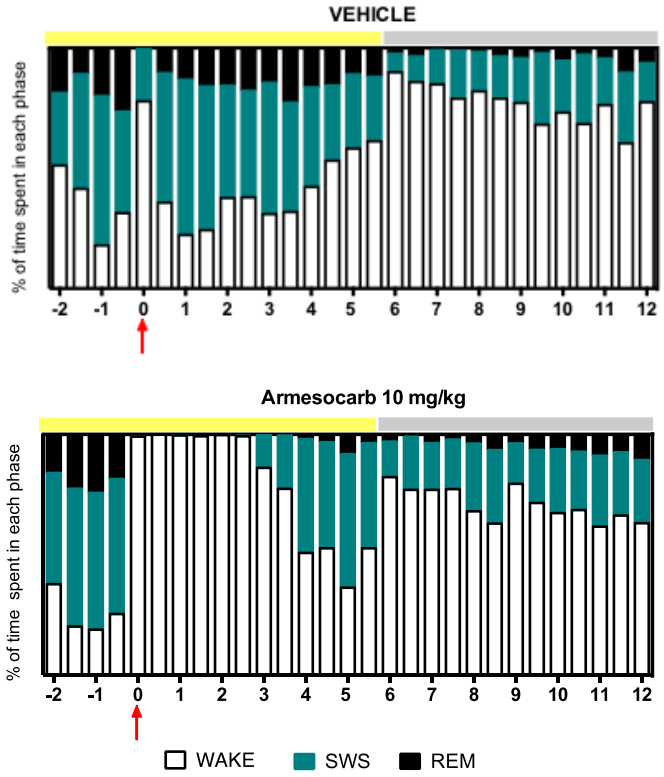
Levodopa is used to relieve the akinesia (motor impairment) symptoms that are characteristic of Parkinson's disease. In the rodent model of Parkinson's disease akinesia is assessed using a forelimb adjusting step test as a measure of functional stepping. Mesocarb given in combination with levodopa, improves motor function (functional steps) beyond what levodopa alone was able to achieve.



Lesioned hemiparkinsonian rats were treated with vehicle, levodopa or a combination of levodopa+ Mesocarb. Forepaw adjusting steps scored and graphed as a percent of the intact (unaffected) forelimb. -Significantly different from the vehicle, P<0.01. NS- not different from the vehicle group.

Mesocarb promotes wakefulness and will be beneficial for patients suffering from daytime sleepiness

Excessive daytime sleepiness is prevalent in ~50% of PD patients and they can fall asleep during driving, a conversation or in a public setting. The effect of MLR-1019 on sleep/wake cycle was assessed using a sleep EEG which measures impaired sleep continuity, disinhibition of REM sleep and changes of non-REM (SWS) sleep and wakefulness. MLR-1019 at 10 mg/kg produced a significant increase in wake time for up to 4 hrs post dosing with the reduction in SWS and REM sleep without adverse effect on EEG power. The wakefulness-promoting effect is comparable to that produced by higher doses of modafinil[5].

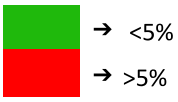


Hypnograms of sleep stages derived from sleep-EEG reveal Mesocarb at 10 mg/kg promotes wakefulness. Dosing occurred approximately 4 hrs into the light cycle and marked with the arrows (time zero). Light and dark cycles are indicated by yellow and grey bars. SWS- slow-wave sleep, REM- rapid eye movement sleep, paradoxical sleep, WAKE – time awake.

3. Safety and Tolerability of MLR-1019

Mesocarb has better reported tolerability than amantadine

		Amantadine	Mesocarb
Top 5 Amantadine AEs (% Observed)	Halucinations	21	<1
	Dizziness	16	0
	Peripheral Edema	16	0
	Dry Mouth	16	0
	Constipation	13	0
Top 5 MLR-1019 AEs (% Observed)	Dysomnia	7	3
	Temporary inappetence	6	3
	Headache	6	3
	Transient BP rise	0	3
	Tachycardia	0	2



The top 5 reported adverse events and the frequency of occurrence for amantadine was taken from the Gocovri® (amantadine) product insert. For Mesocarb data is taken from a collection of published clinical studies collectively reporting 1,298 subjects.

Mesocarb, which was developed in the USSR and sold under name Sydnocarb. It was prescribed for a range of disorders including various asthenic states and those associated with mental retardation, apathy, and reduction in the tolerance to work, anxiety disorders and various sleep disorders. The compound was first approved for use in humans in 1971 and manufacturing was discontinued in 2008 due to business difficulty experienced by the manufacturer.

The use of mesocarb has been described in over 50 publications in a wide variety of clinical contexts, including longitudinal studies up to 2 years in patient cohorts of over 1,000 individuals, including children as early as 7 years of age and geriatric patients. These papers have collectively described the compound as safe and well tolerated. The dose limiting adverse effects were headache, mild blood pressure increases, tension/irritability, and disrupted sleep.

Mesocarb was prescribed for use at doses ranging from 5mg to 150 mg. Melior's studies indicate that the active enantiomer of mesocarb will be efficacious in Parkinson's disease at doses of 3 to 10 mg.

4. Management Team

Andrew Reaume, PhD, President & CEO

Dr. Reaume founded Melior Discovery Inc fourteen years ago and built it into a robust self-sustaining drug discovery organization. He subsequently spun off two sister companies with proprietary clinical stage candidates (Melior Pharmaceuticals I, Inc., Melior Pharmaceuticals II, LLC). As he has grown, first Melior Discovery, and then launched and grown the Melior Pharmaceutical companies he has been responsible for raising over $15 MM of investment capital and completed over $40MM in partnering deals including research partnerships with global pharmaceutical companies. He was responsible for spearheading and continues to oversee a complex global development partnership with an Asian pharmaceutical partner. Dr. Reaume's previous experience includes leadership roles in drug discovery and business analytics at Pfizer and Cephalon with more than twenty-five years of experience in the pharmaceutical industry.

M**ahen Gundecha, BSc, MBA, Chief Business Officer**

Mahen Gundecha is a seasoned health sciences leader with extensive business development, alliance management, new product commercialization and franchise P&L leadership experience across a range of companies, including Juno Therapeutics (Celgene), Novartis Group, Novo Nordisk, Endo Pharmaceuticals and GSK. Mahen has had hands on experience building business development strategies in multiple therapeutic areas and has executed foundational deals. Mahen's most recent experience has involved managing complex global oncology and gene editing partnerships, spanning R&D, manufacturing and commercialization. Mahen brings a broad base of therapeutic experience to Melior, including Neurosciences, Endocrinology, Hematology, Oncology, Rare Diseases, Cell Therapeutics and Gene Editing. Mahen will be leading investment and business development activities at Melior.

Ramana Kuchibhatla, PhD, Senior VP of Clinical Development & Biostatistics

Over the span of his career, Dr. Kuchibhatla has built deep experience in Clinical Development, Biostatistics and Data Management within large and small pharmaceutical companies. He has led filing of multiple INDs and sNDAs, including Zyban® and Lamictal® and has helped to bring several NCEs into clinical development. He was closely involved in several successful in-licensing and out-licensing deals. He is leading development of accelerated clinical development and registration strategies to shorten time to pivotal data read outs. Dr. Kuchibhatla's previous experience includes leadership roles at GSK, Targacept and QED Pharma.

Gennady Smagin, MD, PhD (Head of Preclinical Operations and Development)

Dr. Smagin has more than 15 years of pharmaceutical industry experience, including a broad background in functional neuroanatomy and neurochemistry. Prior to joining Melior, he worked at Lundbeck Research USA (Neuroinflammation Research) and AstraZeneca Pharmaceuticals (CNS/Psychiatry Discovery), where he designed and supervised neurochemical and pharmacological studies in numerous disease areas, including depression, anxiety, Parkinson's (PD) and Alzheimer's (AD) diseases and neurodegeneration. Dr. Smagin received his medical training (MD) from Siberian Medical University (USSR) and a Ph.D. from Pavlov Institute of Experimental Medicine (St. Petersburg, Russia). Dr. Smagin has authored and co-authored over 40 peer-reviewed publications in various areas of neuropharmacology and neuropsychiatry including neurodegenerative diseases, AD, depression, anxiety and schizophrenia.