4/17/13

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Pathologica, through an experienced team of drug hunters, pharmacologists, and regulatory consultants, is developing first-in-class orally-active anti-inflammatory agents with a novel mechanism of action. Clinical proof of concept will be for the treatment of multiple sclerosis. There are currently no approved therapeutics which address the progressive form of multiple sclerosis, a substantially underserved >$3.3B market. PA300, the company's clinical-stage candidate, is strongly efficacious in a clinically-predictive animal model of primary progressive multiple sclerosis, and is unlikely to have the safety issues associated with the currently marketed therapeutics. Pathologica has an FDA-approved IND for pain of osteoarthritis, and is currently planning a subsequent IND filing for multiple sclerosis. Pathologica's PA300 and multiple sclerosis program are protected by strong intellectual property. The company is seeking a partnership for development of PA300.

Pathologica Leadership:

William J. Rutter, Ph.D.
Chairman

Philip Needleman, Ph.D.
Senior Partner

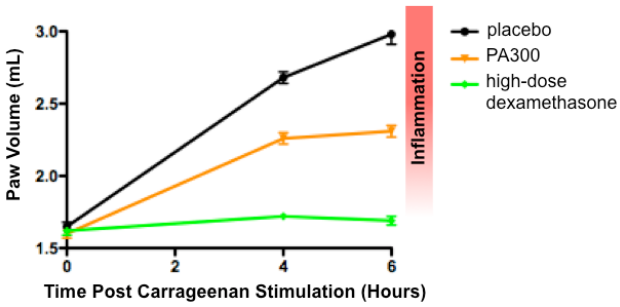
John P. McKearn, Ph.D.
Managing Partner

Jeremy T. Blitzer, M.D., Ph.D.
Partner & VP Product Development

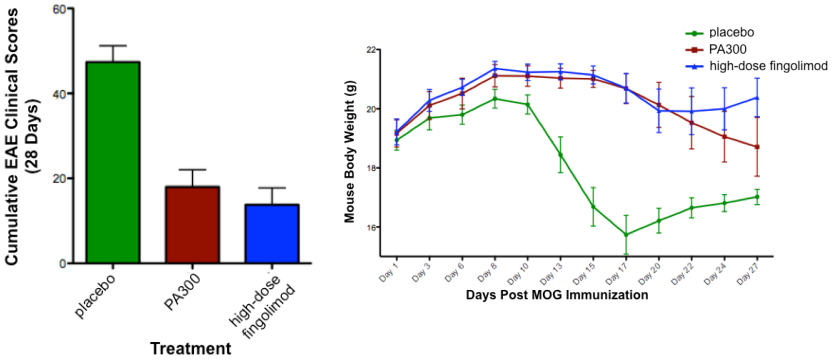
PA300:

PA300 is an orally-active inhibitor of S-adenosylmethionine decarboxylase (a principal enzyme in the biosynthesis of polyamines) which regulates the function of monocytes/macrophages, a key cell population mediating multiple sclerosis. In vitro studies have demonstrated PA300 uptake into monocytes/macrophages with effects on differentiation, but house-keeping processes (e.g. phagocytosis) remain intact. The drug has strong efficacy in a leading animal model of progressive multiple sclerosis (i.e. mouse myelin oligodendrocyte glycoprotein experimental autoimmune encephalomyelitis-MOG EAE), delaying the onset and reducing the overall severity of disease (additional testing in the relapsing/remitting form of the disease is underway). PA300 has a pre-clinical profile suggesting substantial safety advantages over the currently marketed drugs (eg no cytopenias, cardiotoxicity, nephrotoxicity, or hepatotoxicity). Considerable oral bioavailability in humans is expected given demonstration in 5 animal species (mice, rats, dogs, minipigs, and non-human primates).

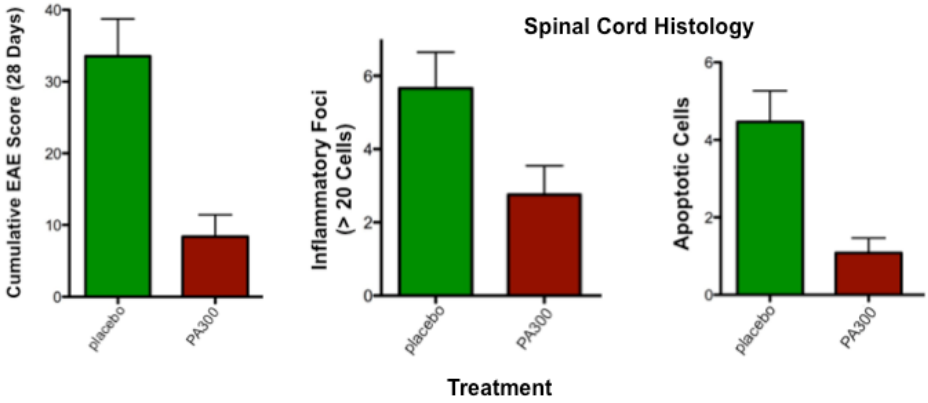
PA300 is Anti-Inflammatory In Vivo
PA300 reduces carrageenan-induced paw swelling in rats.



Mouse MS (MOG EAE) Model: (Study 2 - More Severe Disease than in Study 1)
PA300 reduces cumulative EAE disease burden and prevents EAE disease-associated body weight loss comparably to high-dose fingolimod.



Mouse MS (MOG EAE) Model: (Study 1)
PA300 reduces cumulative EAE disease burden, as well as inflammatory infiltrates and apoptosis in the spinal cord.

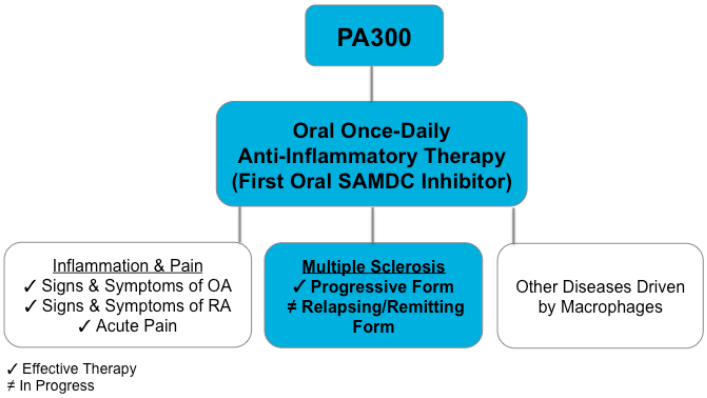


PA300 Toxicology/Safety:
- GLP studies enable dosing up to 14 days in humans (longer-term toxicology studies in near-term, to enable Phase 2a trials in multiple sclerosis)
- No effects on cardiovascular safety pharmacology (e.g. QT interval)
- Non-mutagenic (Ames Assay)
- Non-clastogenic (Chromosome Aberration Assay)
- Clean in vitro pharmacology panel (136/136 receptors, transporters, ion channels, and enzymes)

PA300 Chemistry, Manufacturing, and Controls:
- Facile chemical synthesis
- Substantial GMP quantities manufactured (3 kg scale)
- Stable (30-month official expiration; >5 years of stability demonstrated by requalification)

PA300 Regulatory/Clinical Strategy:
- Efficacy in mouse MOG EAE suggests that PA300 could address primary progressive multiple sclerosis, an under-served disease sub-type with potential orphan designation
- PA300 efficacy assessment in other sub-types of mouse EAE (e.g. relapsing/remitting) is currently underway
- PA300 IND for pain of osteoarthritis is FDA-approved, and near-term Phase 1 program will enable Phase 2a trials in multiple sclerosis
- Team has extensive clinical/regulatory experience in this area

Platform Opportunities:



Comprehensive Pathologica Intellectual Property and Ownership:
- Global rights owned by Pathologica
- Full coverage for oral use of PA300 (20 years plus Hatch-Waxman extensions)
- Coverage of delayed-release formulations of PA300
- Coverage of PA300 analogs
- Claims on methods of treating multiple sclerosis (and other demyelinating and neurodegenerative diseases), pain, and other inflammatory/autoimmune diseases
- Claims on GI-, renal-, and platelet-sparing properties
- Multiple layers of defensive filings

Next Steps:
- Longer-term GLP animal toxicology (up to 3 months) in rats and non-human primates to enable Phase 2a trials in MS
- Phase 2a trial in MS patients

Synergenics Pipeline	Dosage Form	Leads	Pre-clinical Candidate	IND Candidate	Phase I Clinical
Pain/Inflammation (Pathologica)					
PA300 (Polyamine Pathway)	Oral	→	→	→	
	Oral (Enteric-Coated)	→	→	→	
Multiple Sclerosis (Pathologica)					
PA300 (Polyamine Pathway)	Oral	→	→	→	
	Oral (Enteric-Coated)	→	→	→	
Dyslipidemia & Metabolic Disease (BioEnergenix)					
BioE1115 (PAS Kinase)	Oral	→	→	→	

Pathologica is actively seeking strategic partners for development of PA300. Please contact Jeremy T. Blitzer, M.D, Ph.D. (email: jblitzer@synergenics.net; tel: 415-554-8170) for further information.