4/11/13

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Pathologica, through an experienced team of drug hunters, pharmacologists, and regulatory consultants, is developing first-in-class orally-active non-narcotic/non-NSAID GI-, renal-, and platelet-sparing anti-inflammatory drugs with a novel mechanism of action. There is a need for strong, but safer analgesics, and patients with decreased kidney function cannot take traditional NSAIDs or Celebrex given safety considerations. PA300, the company's clinical-stage development candidate, appears as efficacious as Celebrex in clinically-predictive animal pain models, without the safety issues of steroids, traditional NSAIDs, and Celebrex. Pathologica has an FDA-approved IND for pain of osteoarthritis, and is currently seeking a partnership for development of the molecule. Other potential future indications include acute pain and pain of rheumatoid arthritis, as well as inflammatory/autoimmune diseases. Pathologica's PA300 and anti-inflammatory program are protected by strong intellectual property.

Pathologica Leadership:

William J. Rutter, Ph.D.
Chairman

Philip Needleman, Ph.D.
Senior Partner

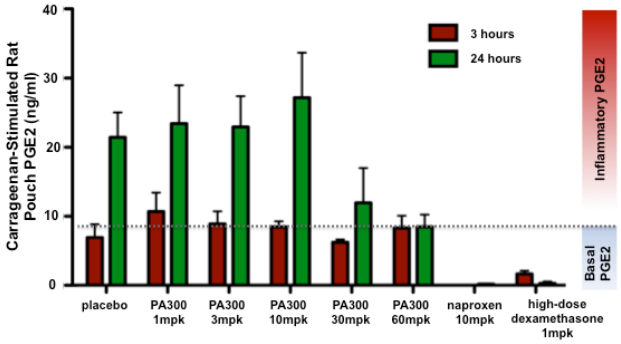
John P. McKearn, Ph.D.
Managing Partner

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

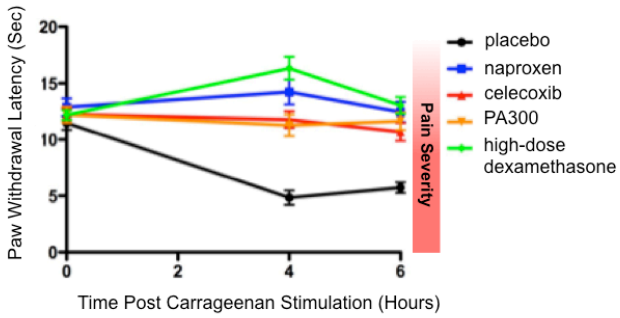
PA300:

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 inflammation. In vitro studies have demonstrated PA300 uptake into monocytes/macrophages with effects on differentiation, but house-keeping processes (e.g. phagocytosis) remain intact. In various rodent models, PA300 has anti-inflammatory/analgesic activity comparable to celecoxib, and suppresses production of inflammatory (pain-driving) prostaglandin E2, while sparing basal levels of this mediator. Given its non-COX1/COX2 mechanism of action, PA300 is also GI-, renal-, and platelet-sparing in animal models. Considerable oral bioavailability in humans is expected given demonstration in 5 animal species (mice, rats, dogs, minipigs, and non-human primates).

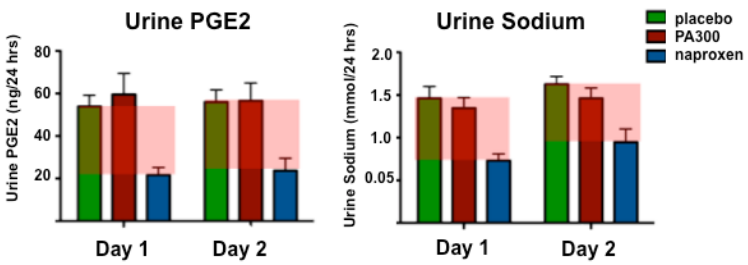
Rat Carrageenan Air Pouch
PA300 selectively inhibits inflammatory PGE2, sparing basal levels (naproxen & dexamethasone inhibit both forms).



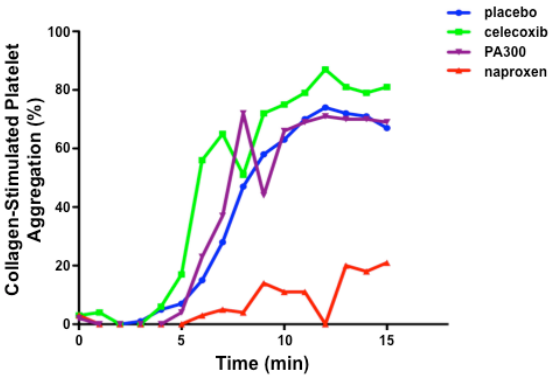
Rat Carrageenan Paw Hyperalgesia
PA300 & celecoxib reduce pain with comparable efficacy.



Rat PA300 Renal-Sparing Pharmacology
PA300 has no effect on renal-derived PGE2 and sodium excretion, in contrast to naproxen.



Rat PA300 Platelet-Sparing Pharmacology
PA300 (and celecoxib) have no effect on platelet aggregation.



Toxicology/Safety:

- GLP studies enable dosing up to 14 days in humans (sufficient for Phase 2a in pain and renal-sparing assessments)
- Wide safety margins
- 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)

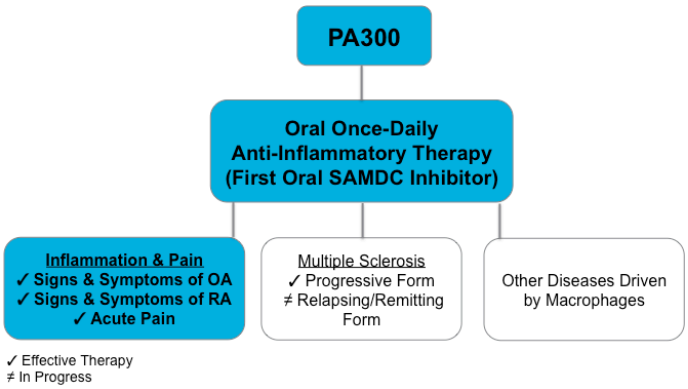
PA300 Chemistry, Manufacturing, and Controls:

- 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:

- Equivalent efficacy to Celebrex and GI-, renal-, and platelet-sparing properties suggest that PA300 could be a fully-differentiated anti-inflammatory agent at least as good as leading marketed drugs without their inherent safety liabilities
- Pain of osteoarthritis will be initial indication (straight-forward path to proof-of-concept and registration)
- Initial IND is FDA-approved and 12-month plan includes 2 Phase 1 trials (single and multiple ascending dose) and 2 Phase 2 trials (efficacy in osteoarthritis and upper GI safety; renal safety in healthy elderly volunteers)
- Other potential future indications include acute pain, pain of rheumatoid arthritis, and inflammatory/autoimmune diseases
- Team has extensive clinical/regulatory experience in these areas

Platform Opportunities:

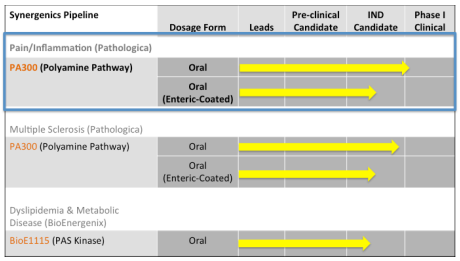


Comprehensive Pathologica Intellectual Property and Ownership:

- Global rights owned by Pathologica
- Full IP 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 pain, multiple sclerosis, and other inflammatory/autoimmune diseases
- Claims on GI-, renal-, and platelet-sparing properties
- Multiple layers of defensive filings

Next Steps:

- 4 clinical trials: Phase 1a single ascending dose and Phase 1b multiple ascending dose studies in healthy volunteers; two Phase 2 trials (in osteoarthritis patients to demonstrate PA300 efficacy and upper GI safety; in healthy elderly volunteers to demonstrate the PA300 renal-sparing property)



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.