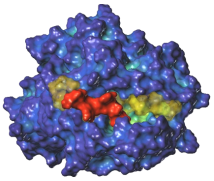
December 2019

Provid identifies promising second-generation drug candidates for MS with high potency, superior pharmacokinetics and long IP timespan. The developments are described in the company's Executive Summary

PROVID
Pharmaceuticals



Breakthrough Drug Candidates for Autoimmune Disease
DRB1*15:01 Inhibitors for Multiple Sclerosis

*Provid Pharmaceuticals Inc. has discovered novel, small molecule therapeutics for the treatment of multiple sclerosis. The PV compounds are potent and exquisitely selective blockers of the disease-associated MHC class II molecule DRB1*15:01. The efficacy of the Provid compounds has been demonstrated in animal models of MS and in human cellular assays. Efficacy has also been shown in models of Goodpasture's disease, a rare kidney autoimmune disease also linked to DRB1*15:01. Based on the data and initial ADMET studies of the initial lead PV-267 and novel, second-generation optimized analogs, Provid is seeking a partner or investors to complete IND-enabling studies, to initiate clinical trials, and to pursue downstream development and commercialization.*

Provid's MS drug candidates uniquely and specifically inhibit the MHC Class II molecule DRB1*15:01, the most important gene target in the autoimmune disease process in MS. The DRB1*1501 molecule is carried by a majority of MS patients. DRB1*15:01 binds and presents antigenic myelin fragments to autoreactive T cells, triggering the autoimmune response that leads to damage to the myelin insulation on nerves, resulting in MS disease pathology. Provid leads bind exclusively to DRB1*15:01, blocking antigen binding and T-cell activation but, unlike all other MS drugs is otherwise immunologically inert. This specificity is an important safety factor compared to existing MS drugs that have serious safety concerns due to their disruption of normal immune pathways. The initial lead analog, PV-267, is effective in MS models in DRB1*15:01 transgenic mice and both PV-267 and 2nd generation analogs are active in human cells from DRB1*15:01-positive MS patients, studies performed by our collaborator, Prof. T. Forsthuber at UT San Antonio. Novel 2nd generation compounds show improved stability and PK properties have been selected for further development.

Commercial and Clinical Opportunities. The market for MS drugs worldwide in 2018 exceeded $20 billion. There is a clear medical need and huge market opportunity for a superior MS drug with enhanced safety. The Provid compounds would be expected to garner over $4 billion in annual sales based on their profile. The DRB1*15:01 antagonists would direct the therapy only to patients who carry the DRB1*15:01 gene and thus the most relevant disease mechanism. Simple diagnostic tests can be used to select DRB1*15:01-positive MS patients who would benefit from PV treatment, strengthening clinical trial outcomes and affording a pathway for approval for first-line therapy. The mechanism of blocking DRB1*15:01 also creates opportunities for biomarkers to assess mechanistic efficacy in early clinical trials and would simplify phase II/III trials. Our initial lead PV-267 has also shown promising activity in models of Goodpasture's disease, a rare, kidney disease with DRB1*15:01 genetics, in studies by Drs. J. Ooi and R. Kitching at Monash University (Melbourne, AU).

The Provid compounds are unique in their potential for high efficacy in MS coupled with superior safety compared to current drugs. Established first-line MS drugs (interferons, glatiramer) are only moderately effective and produce troublesome side effects. Some newer, "disease-modifying" drugs have greater efficacy, but carry a high risk of compromising the normal immune system, risking catastrophic infections and death. Oral drugs (dimethyl fumarate, fingolimod) and potent biologics targeting B cells have recently become available. Their improved efficacy in treating patients is compromised by serious safety issues.

Recent data have shown that the initial lead, PV-267, has high oral bioavailability in a proprietary formulation being developed in collaboration with Enteris Biopharma. Oral efficacy would be a commercial advantage and convenience for MS patients. Studies with the 2nd generation compounds are planned.

Early Clinical Proof-of-Concept. Because of its pure DRB1*15:01 antagonist mechanism, we plan to assess *immunological efficacy* in DRB1*15:01-positive MS patients in early clinical trials, greatly reducing the clinical development risk and clearing the path for targeted phase II efficacy trials. These studies are being planned in consultation with our Clinical Advisory Board led by Prof. Lawrence Steinman of Stanford University.

Partnerships, Funding, Commercialization, and Patents. The development of the PV inhibitors has been financed by the company, by NIH grants, by funding from Fast Forward, the venture philanthropy arm of the National MS Society, and by the NJ Economic Development Authority. Patents on composition of matter and methods of use are issued. New patent applications on 2nd generation analogs will afford 20+ years of patent life.

Contacts:
Gary L. Olson, PhD, President & CEO, Provid Pharmaceuticals Inc., gary.olson@provid.com
Lawrence Poster, Managing Director, Catalyx Group, lposter@catalyx.com