

ATI-9242 for Psychiatric Disorders

PRODUCT OVERVIEW

ATI-9242 is designed to be a novel, next-generation atypical antipsychotic for the treatment of schizophrenia and other psychiatric disorders. We believe this product will improve upon the efficacy of the best atypicals while avoiding metabolic drug-drug interactions and minimizing certain other metabolic problems associated with atypicals, including weight gain and type 2 diabetes. The receptor profile of ATI-9242 is designed to treat negative symptoms of schizophrenia and enhance cognitive functions. We entered the clinic with ATI-9242 in April 2008.

LIMITATIONS OF CURRENTLY MARKETED ANTIPSYCHOTICS

Common side effects shared by first-generation antipsychotic drugs include involuntary muscle contractions, cardiovascular effects, and sedation. Long-term use of these agents can effect menstrual cycles or sexual function and can cause movement disorders such as tardive dyskinesia. Second-generation antipsychotics (“atypicals”) are associated with serious and potentially fatal adverse effects. Clozapine, the first atypical antipsychotic, is associated with agranulocytosis, or a serious reduction in white blood cells, in 0.5%-1% of patients, and seizures in about 2% of patients. In addition, clozapine and other atypicals can be associated with weight gain, type-2 diabetes, sedation, and orthostatic hypotension which results in a significant loss of blood pressure when moving from sitting or lying to a standing position. None of the currently available atypicals adequately addresses the negative symptoms – reduction in social interaction, disassociation from people or settings, monotone speech, loss of feelings of pleasure – and the cognitive deficit associated with schizophrenia.

ATI-9242 PRE-CLINICAL STUDIES

In vitro receptor profiling has demonstrated that ATI-9242 has moderate D₂ receptor affinity and a high 5HT_{2A}/D₂ binding ratio characteristic of atypical antipsychotic agents. In addition, ATI-9242 binds with high affinity to the 5HT₇ receptor and exhibits 5HT_{1A} partial agonist activity. In rat cortical neurons, ATI-9242 potentiates NMDA current and facilitates GABAergic neurotransmission. In rats, it increases dopamine and acetylcholine in the prefrontal cortex, with no measurable increase in the nucleus accumbens.

ATI-9042 RECENT DEVELOPMENT MILESTONES

- ✓ Completed IND Submission 1Q 2008
- ✓ Initiated human safety trial 2Q 2008

This document contains forward looking statements. For a full description of our business and its associated risks, please refer to our filings with the Securities and Exchange Commission. We assume no obligation to publicly update any information or statement contained in this document. Updated April 2008. © ARYx Therapeutics, Inc.

ATI-9242 AT-A-GLANCE

- In development for treatment of schizophrenia and other psychiatric disorders
- Designed for enhanced safety vs. currently marketed antipsychotics
 - Improved metabolism
 - Reduced metabolic side effects

ATI-9242 TARGET PROFILE

- Treatment of both the positive and negative symptoms of schizophrenia
- Superior efficacy vs. currently marketed therapies in the treatment of cognitive symptoms
- Once-a-day oral dosing
- 100x safety margin at therapeutic doses
- Reduce metabolic problems associated with existing atypicals such as weight gain and type 2 diabetes

ABOUT SCHIZOPHRENIA

- Chronic disorder afflicting up to 1% of the world’s population.
- Afflicts ~3.2 million people in the US
- Cost of care estimated at 2.5% of annual US health care expenditures
- Global sales of antipsychotics >\$15B (2006)

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