

## Novel Therapies for Patients with Autism and Fragile X Syndrome

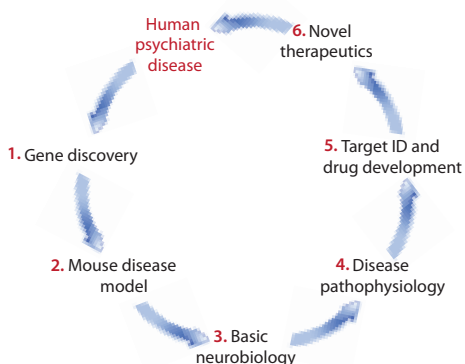
Seaside Therapeutics is creating new drug treatments to correct or improve the course of Fragile X Syndrome, autism and other disorders of brain development. We are dedicated to translating breakthrough discoveries in neurobiology into therapeutics that improve the lives of patients and their families.



### Translating Breakthrough Science into Therapeutics

Seaside Therapeutics understands the toll that brain development disorders, including autism and intellectual disability, take on families and share the sense of frustration that effective therapeutics are not available despite recent scientific advances. Historically, drug discovery in disorders of brain development has been unproductive largely due to the lack of a mechanistic understanding of these disorders, as well as the absence of predictive animal models. Seaside is changing this paradigm through scientific exploration that focuses on identifying the fundamental pathophysiology of brain development disorders and application of this knowledge to develop targeted therapeutics. A key advance for understanding Fragile X Syndrome was the discovery of the specific genetic cause and subsequent engineering of a relevant mouse disease model. Through study of these genetically engineered mice, Seaside founder Dr. Mark Bear and his colleagues discovered a molecular pathway, an mGluR signaling cascade, that is disrupted in a specific disorder of brain development – Fragile X Syndrome. Further research has provided insights for developing novel medications to normalize the function of this pathway, which Seaside believes may extend beyond Fragile X Syndrome into a number of other developmental disorders, including autism.

### FULFILLING THE GOAL OF MOLECULAR MEDICINE THROUGH RESEARCH IN FRAGILE X SYNDROME



1. Discovery that *FMR1* gene is silenced in Fragile X Syndrome
2. Creation of *Fmr1* knockout mouse
3. Discovery of exaggerated mGluR5-dependent protein synthesis in Fragile X mouse
4. Diverse disease phenotypes linked to increased mGluR5 signaling
5. Seaside focuses research on pharmacological correction of mGluR5 signaling
6. Seaside introduces STX107 and STX209

### FRAGILE X PROGRAM

Fragile X Syndrome is the most common inherited form of mental impairment and the most common known cause of autism. There is no cure for Fragile X Syndrome at this time, and the current standard of care focuses on treating specific symptoms such as anxiety, or improving and controlling behavior. Seaside has two candidates in development for the treatment of Fragile X Syndrome: STX209, which is currently in a Phase 2 open label clinical trial in children, adolescents and adults with Fragile X Syndrome; and STX107, which will commence enrolling individuals with Fragile X Syndrome in a Phase 2 trial in the second half of 2010. Data from the Phase 2 STX209 study is expected in the first half of 2010.

### AUTISM PROGRAM

Although a variety of medications and behavioral interventions are used in an attempt to address individual symptoms of the disease, there is no cure for autism. Seaside is developing STX209 for the treatment of autism and a Phase 2 clinical trial in adolescents with autism spectrum disorders is currently enrolling patients. Data from this open label study is expected in the first half of 2010.

More information for patients and families affected by these disorders can be found at the Company's website: [www.seasidetherapeutics.com](http://www.seasidetherapeutics.com).

## CLINICAL STAGE CANDIDATES

Seaside's drug development efforts are focused on creating new treatments to correct or improve the course of Fragile X Syndrome and autism.

### STX209: Fragile X and Autism

STX209 has demonstrated efficacy in preclinical studies and has successfully completed a Phase 1 study in healthy volunteers. This compound reduces glutamate signaling in the brain and should, thereby, indirectly inhibit excessive metabotropic glutamate receptor (mGluR) mediated protein synthesis.

#### Program Status

- Phase 2 clinical trial in adolescents and adults with Fragile X Syndrome has completed enrollment; data is anticipated in the first half of 2010
- Phase 2 clinical trial in adolescents and adults with autism spectrum disorders is actively enrolling patients; data is anticipated in the first half of 2010

### STX107: Fragile X

STX107 has completed investigational new drug (IND) enabling studies and Seaside opened an IND with the Food and Drug Administration in August 2009. In-licensed from Merck, STX107 is a highly potent, selective metabotropic glutamate receptor subtype 5 (mGluR5) antagonist. Evidence suggests that many of the neurological and psychiatric consequences of Fragile X Syndrome result from exaggerated signaling through mGluR5 receptors.

#### Program Status

- Phase 2 trial in individuals with Fragile X Syndrome is expected to begin enrolling patients in the second half of 2010

## ADDITIONAL INDICATIONS

A number of other developmental disorders are associated with similar core characteristics of autism and Fragile X Syndrome including developmental delay, cognitive impairment, repetitive behavior and anxiety. We anticipate that some of these disorders also have exaggerated mGluR signaling and that some of the patients impacted by these disorders may receive therapeutic benefit from treatment with STX107 and/or STX209.

## A COLLABORATIVE APPROACH

Seaside believes that significant advances in the treatment of developmental brain disorders will be facilitated and progress expedited through extensive research partnerships and collaborations. The Company has strategically partnered with pharmaceutical and biotechnology companies, universities, government agencies, foundations and advocacy groups to assemble the assets and resources necessary for success. Seaside is the recipient of an NIH cooperative agreement awarded to support translational research in cooperation with scientists from NIMH, NICHD, NINDS, BPCA, FRAXA and Autism Speaks.

#### Partnerships include:

- Autism Speaks
- Baylor College of Medicine
- Correlagen Diagnostics, Inc.
- FRAXA Research Foundation
- Merck & Co., Inc.
- Vanderbilt University Medical Center



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