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CPP-115 FOR REFRACTORY COMPLEX PARTIAL SEIZURES AND INFANTILE SPASMS

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Catalyst is developing a GABA-aminotransferase (GABA-AT) inhibitor, CPP-115, for the treatment of refractory complex partial seizures and infantile spasms. The indications for this new drug are based on its identical mechanism of action compared to vigabatrin, an approved drug for these indications, marketed under the trade name Sabril®. CPP-115 is a patent protected new molecular entity. CPP-115 is significantly more potent than vigabatrin and will likely cause less visual field defects. Therefore, Catalyst believes CPP-115 has the potential to be a safer, next generation, replacement for vigabatrin as an anticonvulsant and it is also being developed for the treatment of substance abuse.

CPP-115 is being evaluated in the NIH's Anticonvulsant Screening Program (ASP). Data comparing CPP-115 and vigabatrin are available in two variants of the 6 Hz minimal clonic seizure model in mice (at both 32 mA and 44 mA, 3 second, stimuli) and in a corneal kindled model in mice (8 mA, 60 Hz, 3 seconds, for 8 days to achieve at least bi-daily stage 5 seizures). In a comparison of the two drugs, CPP-115 was found to be about 4-5 times more potent. CPP-115 was also found to be effective in a maximal electroshock model. Although CPP-115 again appears more potent, a quantitative comparison is not possible due to differences in experimental parameters for the vigabatrin testing reported in the literature. CPP-115, like vigabatrin, was found to be ineffective in a number of other models. In summary, the epilepsy models in which CPP-115 is effective match vigabatrin, but at a higher potency. CPP-115 was also found to be initially sedating at a dose that is closer to the effective dose than vigabatrin (a narrower therapeutic index). Like vigabatrin, the sedative effect resolves completely in about 2 weeks. Therefore, CPP-115 will require a dose titration at the initiation of therapy similar to the titration that is recommended in the labeling for vigabatrin.

Catalyst has completed non-clinical tests for target specificity (no clinically significant effect on 111 of the most common pharmacological targets, no binding to any GABA receptors or transporter subtypes, and no binding to SSADH). Unlike vigabatrin, CPP-115 also does not inhibit other transaminases (specifically, ALT and AST). CPP-115 does not induce or inhibit the most common CYP enzymes and it is not metabolized by human hepatocytes. No genotoxic potential was detected in the Ames and chromosomal aberration tests and it does not inhibit the hERG channel. Finally, it is rapidly and completely absorbed and rapidly eliminated, with predicted human pharmacokinetics similar to vigabatrin's. The drug causes no observable effects on cardiovascular function, respiration, or CNS (other than the sedation at elevated doses).

Catalyst has also evaluated CPP-115 compared to vigabatrin in a 90 day vision safety test in Wistar rats. CPP-115 was found to cause 65%-85% less visual field damage (as determined by ERG testing) than vigabatrin. Histological evaluation of the retinas is ongoing with results expected in Q2 2011. Based on the results observed in this test for both drugs and the correlation to the development of visual field defects in people treated with vigabatrin, Catalyst believes the incidence of visual field loss from the use of CPP-115 will likely be significantly reduced, and the progression of visual field loss that does occur will likely be slower.

CPP-115 is protected by two composition of matter patents, expiring in 2023, and as a new molecular entity, extension to 2028 under the Patent Term Restoration Act is anticipated. CPP-115 has been granted orphan drug designation for infantile spasms. The remainder of the IND enabling studies will be completed in the summer of 2011 and IND filing and the initiation of Phase 1 human safety testing are expected in Q3 2011.