THE 5-ANTIGEN TRANSPORT-INHIBITING Oligonucleotide POLYMER (STOPS™) ALG-010133 DEMONSTRATES A FAVORABLE NONCLINICAL PHARMACOKINETIC AND TOXICOLOGY PROFILE FOR THE TREATMENT OF CHRONIC HEPATITIS B (CHB)

Misner, DL\textsuperscript{1}, Gohil, V\textsuperscript{2}, Zhang, Q\textsuperscript{3}, Slater, C\textsuperscript{2}, Wojcinski, Z\textsuperscript{3}, Venkatraman, M\textsuperscript{4}, Chen, A\textsuperscript{2}, Rajwanshi, VK\textsuperscript{5}, Williams, C\textsuperscript{1}, Fry, J\textsuperscript{2}, Smith, DB\textsuperscript{5}, Symons, JA\textsuperscript{2}, Blatt, LM\textsuperscript{5}, Beigelman, LN\textsuperscript{5}, Lin, T\textsuperscript{6} and Chanda, SM\textsuperscript{1}

\textsuperscript{1}Aligos Therapeutics, Inc.; \textsuperscript{2}Charles River Lab.; \textsuperscript{3}Tox. & Path. Consult., LLC; \textsuperscript{4}Aligos Belgium BV; \textsuperscript{5}Corresponding author: dmisner@aligos.com

Background

Current standard of care for CHB viral infection can effectively inhibit viral DNA replication but fails to reduce HBsAg. Nucleic acid polymers have been reported to reduce circulating HBsAg in CHB patients. We have identified STOPS that contain novel chemical features, providing enhanced potency in several HBV cell lines.

Methods

ALG-010133 was generally formulated in water for injection. CD-1 mice and cynomolgus monkeys were dosed subcutaneously (SC), or by intravenous infusion (IV) in monkeys, to assess the pharmacokinetic properties of ALG-010133. Repeat dose toxicity studies were conducted in mice and monkeys administered weekly (QM) SC for 2-13 weeks, and with twice weekly (BMW) dosing for 2 weeks followed by weekly dosing in 6- or 9-month chronic mouse or monkey toxicology studies. Reproductive toxicology studies were conducted in mice and NZW rabbits with twice weekly or every other day dosing. Reproduction and maternal toxicity studies were conducted in mice up to 50 mg/kg/dose.

Sustained ALG-010133 exposure in liver following a single SC dose in mice and monkey with good bioavailability following single SC dosing in monkeys

Dose- and time-related increase of ALT observed in mice after 12-weeks at 15 and 50 mg/kg/dose but no significant ALT elevation in mice after 26-weeks up to 3 mg/kg/dose

No adverse findings in embryofetal development or fertility studies noted

Conclusions

The combination of PK properties to enable SC administration along with a favorable safety profile allowed advancement of ALG-010133 into clinical development to be evaluated as a potential treatment for CHB. The lack of efficacy after 12-weeks of dosing in CHB subjects resulted in the termination of ALG-010133 for CHB treatment.

References


Financial disclosures: All authors are employees of Aligos Therapeutics, Inc., or were contracted by Aligos Therapeutics, Inc., to conduct studies on their behalf.