AMB-051-02 STUDY SUMMARY

Study Sponsor: AmMax Bio, Inc.

Protocol Number: AMB-051-02

Study Title: A Phase 2, Adaptive, Open-Label, Multiple-Dose, Dose Escalation Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of Intravenous AMB 05X in Subjects with Tenosynovial Giant Cell Tumor

Study Initiation Date (First Subject In): 16 September 2021

Date of Early Study Termination: 03 November 2021

Study Completion Date (Last Subject Last Visit): 14 April 2022

Objectives:

The objectives of this study were to evaluate the safety, efficacy, and pharmacokinetics (PK) of intravenous (IV) AMB-05X in the treatment of Tenosynovial Giant Cell Tumor (TGCT).

Methodology:

This was a Phase 2, open-label, multiple-dose, dose-escalation study with an adaptive design that was to enroll up to up to 48 subjects with TGCT into up to 6 serial dose cohorts. The study consisted of a screening period of up to 4 weeks, a treatment period of 12 weeks, and a post-treatment follow-up period of 12 weeks. Each subject received a dose of open-label IV AMB-05X every 2 or 4 weeks, for a total of 6 or 3 doses over the 12-week treatment period. Dosing began with an initial 3 subjects in Cohort A at an initial priming dose of 4 mg/kg on Day 1 followed by 5 maintenance doses of 2 mg/kg administered every 2 weeks (at Weeks 2, 4, 6, 8, and 10). The dose levels and regimens for subsequent cohorts were to be determined by the Sponsor Data Monitoring Committee (DMC) based on an ongoing analysis of available safety, tolerability, PK, pharmacodynamics (PD) and efficacy data from the previous cohort(s).

Number of Subjects Enrolled and Analyzed:

A total of 4 subjects were enrolled and treated.

- 4 subjects were included in the Safety and modified Intent-to-Treat (mITT) Populations.
- 3 subjects were included in the Per-Protocol (PP) Population.

The study was stopped early in November 2021 to focus more on AMB-05X intra-articular administration. No safety or other clinically related concerns were noted.

Gender: Male or female **Age:** ≥18 years

Diagnosis and Main Criteria for Eligibility:

Subjects with TGCT histologically confirmed by a pathologist.

Subjects with measurable disease with a minimum size of 2 cm defined by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, assessed from magnetic resonance imaging (MRI) scans by a central radiologist.

Safety:

Safety was evaluated using the following assessments: AEs/SAEs, concomitant medications, body weight, vital signs, physical examination, electrocardiogram (ECG), pregnancy tests, clinical laboratory tests, and tolerability assessment.

Efficacy:

Efficacy was evaluated using the following assessments:

- MRI and central radiologist assessment of tumors based on RECIST v1.1 and tumor volume score (TVS)
- Clinician evaluation of range of motion (ROM) in the affected joint
- Patient-Reported Outcomes: Measurement Information System (PROMIS) Physical Function Scale, Worst Stiffness numeric rating scale (NRS), Brief Pain Inventory (BPI) Short Form (including the Worst Pain NRS item), and EuroQol 5 Dimension 5 Level

Statistical Methods:

Safety Population: All subjects who received at least 1 dose of study drug.

mITT Population: All subjects who received at least 1 dose of study drug and had both baseline and post-baseline data for at least 1 efficacy endpoint.

PP Population: Subjects in the mITT Population who completed the study and did not have protocol deviations that could significantly affect the interpretation of the endpoints.

All study data are listed because of the small number of subjects.

Disposition:

All 4 subjects received the initial priming dose of 4 mg/kg and completed the study; however, 1 subject discontinued study drug early. No subjects withdrew consent from the study. One subject was enrolled and treated, and later found to have TGCT with malignant transformation; and was therefore excluded from the PP Population (n=3).

Efficacy Results:

All 3 subjects in the PP Population had stable disease as determined by RECIST v1.1 and TVS. Two subjects had an increase in joint ROM. At Week 12, the mean changes from Baseline in PROMIS, BPI, and worst stiffness scores were primarily a range of no mean changes to small mean changes in the PP Population during the study.

Pharmacokinetic, Pharmacodynamic, and Anti-Drug Antibody Results:

Peak serum levels across the study period were observed at the 2-hour post-infusion time point, consistent with the loading dose and lower maintenance dose regimen. Moreover, no apparent accumulation was observed between Weeks 2 and 10.

With regards to colony-stimulating factor 1 (CSF1) levels as a PD marker of CSF1 receptor (CSF1R) occupancy and native ligand blocking by AMB-05X, concentrations increased 10-fold within 2 hours of AMB-05X infusion and peaked to another 10-fold higher level just before the second drug infusion and remained stable at that level for the remainder of the treatment period.

One subject was determined to have detectable anti-drug antibody (ADA) activity at Baseline and Visit 7 (Week 10) although the titer was relatively low and slightly higher at Baseline than at Visit 7. PK was not altered. Therefore, no apparent generation of ADA was evident in this study.

Safety Results:

No subjects had any dose reductions, dose interruptions, or infusion-site reactions. All 4 subjects had Grade 1 or 2 face edema; none were considered severe; 3 of the 4 subjects had events that were considered related to study drug. Two subjects had a Grade 3 AE (hypertension considered related to study drug and acute pyelonephritis considered not related to study drug).

One subject had three Grade 1 AEs that led to treatment discontinuation (face edema, increased hepatic enzyme, and epistaxis). All 3 events were considered related. No deaths or SAEs were reported in the study.

The following laboratory abnormalities were reported as AEs: increased hepatic enzyme, increased blood lactate dehydrogenase, and increased aspartate aminotransferase. One subject had an AE of skin hyperpigmentation. Otherwise, no clinically significant changes were observed in chemistry, hematology, urinalysis, vital signs, physical examination findings, or ECGs.

Conclusions:

- The AEs observed in this study were those expected for this drug class.
- PK, PD, and ADA results are consistent with prior results.
- No unexpected or new efficacy or safety findings were observed in this study.