**AT1412, a Patient-Derived Antibody in Development for the Treatment of CD9 positive B-Acute Lymphoblastic Leukemia**

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**Background**
- AT1412 was isolated using AIMSelect from B cells of a patient who was cured of stage IV metastatic melanoma
- AT1412 is a fully human patient derived IgG1 antibody that targets CD9.
- CD9 is overexpressed on many different types of tumor, making it an attractive target for immunotherapy.
- AT1412 binds CD9-expressing tumor cells including melanoma and gastric, colon- and pancreatic cancer.
- AT1412 is able to control human melanoma growth in vitro and in mice (Abstract #1310 Poster #532).
- In B-ALL, CD9 is expressed in 60-80% of cases and correlates with an adverse prognosis.
- Here we explore the efficacy of AT1412 for potential treatment of B-ALL.

**1. AT1412 targets CD9 on platelets but does not cause platelet aggregation in contrast to other anti CD9 antibodies**

(A) Platelet Rich Plasma was incubated with AT1412. Antibody binding was visualized by secondary anti-human IgG A647 staining and flow cytometry.

(B) Whole blood was incubated with indicated stimuli at 37 °C under stirring conditions. Thrombocyte aggregation assessed by impedance aggregometry.

**2. AT1412 binding correlates with level of ADCC of patient-derived B-ALL**

(A) AT1412 binding of primary B-ALL samples as detected by flow cytometry. Binding ratio of AT1412 over isotype control of B-ALL versus T-ALL samples: **p<0.0001** (Mann-Whitney test)

(B) Binding of AT1412 versus AT1412 mediated cytotoxicity on patient B-ALL samples. Binding is represented as MFI of AT1412 subtracted by the MFI of isotype control. The percentage of ADCC is corrected for isotype control cell death: **p<0.001** (Spearman r)

3. **AT1412 does not induce thrombosis, but does induce transient thrombocytopenia in cynomolgus monkeys, without increased the risk of bleeding or other signs of toxicity**

Cynomolgus monkeys were dosed with a single infusion of AT1412 (3, 5, or 10 mg/kg). Blood was drawn at indicated timepoints to determine (A) platelet counts and (B) coagulation parameters.

4. **AT1412 reduces B-ALL tumor burden in human immune system mice**

Mice carrying a human immune system xenografted with luciferase expressing human SUP-B15 B-ALL cells, were treated twice per week intravenously with AT1412 or isotype control antibody. Bioluminescence in isolated organs was determined after sacrifice. (Kruskall Wallis with Dunn’s multiple comparisons test)

**Conclusion**

AT1412
- Is a fully human patient derived IgG1 antibody targeting CD9.
- Induces ADCC in CD9-expressing B-ALL cells and controls B-ALL growth in human immune system mice.
- Does not induce thrombocyte aggregation, which is in sharp contrast to previously described CD9 antibodies.
- Induced transient thrombocytopenia in non-human primates without increased risk of bleeding and bruising.
- AT1412 does not induce any other signs of toxicity in humanized mice or in non-human primates.
- AT1412 is currently in preclinical development. First in Human studies are scheduled to start Q1 2021.

Conflict of interest disclosure:

RS, JV, SL, DG, EF, MF, SH, DB, CF, MK, YC, PVH, HS are employees of AIMM Therapeutics.

RS, JV, SL, DG, EF, MF, SH, DB, CF, MK, YC, PVH, HS, RV have equity ownership in AIMM Therapeutics.

RS, WP, DG, JV, CF, PVH, HS are inventors on a patent relevant to this subject.

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