

HuABC2: A Humanized Anti-CD122 Antibody for Treatment of Immune-Mediated Diseases

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Summary: HuABC2 is a humanized IgG antibody against CD122 (β chain subunit shared by IL-2 receptor and IL-15 receptor) that can block the action of both IL-2 and IL-15. HuABC2 and its surrogate anti-mouse CD122 antibody (ChMBC7) reduced NK and CD8+ memory T cells, but not Treg cells, in vivo. HuABC2 was effective for prevention of renal allograft rejection with no major adverse events in non-human primates. ChMBC7 was shown to be therapeutically efficacious in the mouse models of vitiligo, type 1 diabetes, and skin allograft rejection. Anti-CD122 treatment has also been reported to be effective for alopecia areata and Celiac disease in mice. Taken together, HuABC2 will be a promising antibody drug for immune-mediated diseases.

Background: CD122, a 525 amino acid-long membrane protein expressed on T cells, NK cells and monocytes, is an integral part of the receptor for IL-2 and IL-15. CD122 combines with other receptor sub-components to generate receptors that differ in specificity and affinity. CD122 in combination with CD132 forms a receptor with an intermediate level of affinity for both IL-2 and IL-15. CD122 associated with both CD25 and CD132 results in a receptor with very high affinity specific for IL-2, while a complex of IL-15 and CD215 binds to the CD122/CD132 receptor with a high affinity.

The Antibody: HuABC2 is a high affinity humanized IgG1/kappa monoclonal antibody against human, rhesus and cynomolgus CD122. HuABC2 was generated and humanized at JN Biosciences, thus has no third party encumbrances. A surrogate rat/mouse chimeric anti-mouse CD122 antibody ChMBC7 was also generated at JN Biosciences and has been used widely by academic collaborators.

The Opportunity: JN Biosciences is seeking a licensee for clinical development and commercialization of HuABC2. Please send inquiries to Jade Brown at JB Jade1996@aol.com.

Highlights of Preclinical Studies:

Mouse vitiligo model (Richmond et al., Sci. Trans. Med. 10:eaam7710, 2018)

- Anti-CD122 (ChMBC7) reversed disease in mice with established vitiligo.
- Short-term treatment with ChMBC7 provided durable repigmentation when administered either systemically or locally in the skin.

Mouse type 1 diabetes model (Yuan et al., JCI Insight 3: e96600, 2018)

- Anti-CD122 (ChMBC7) selectively ablated NK and CD8+ T cells from pancreatic islets.
- Treg cells in the islets were not affected by ChMBC7 treatment.
- CD122 blockade restored immune tolerance in type 1 diabetes.

Mouse skin allograft model (Mathews et al., J. Clin. Invest. 128:4557-4572, 2018)

- Combination of anti-CD122 (ChMBC7) with costimulation blockers (CoB; CTLA4-Ig and anti-CD154), in comparison to CoB alone, significantly prolonged skin allograft survival.

Monkey PK/PD/safety study (Landofi et al., poster presentation at the FOCIS 2012 meeting)

- HuABC2 was well tolerated with no major adverse events.
- HuABC2 prevented renewal of NK and CD8+ T cells.
- Significant occupancy of CD122 by a single dose of HuABC2 persisted over 14 days.

Monkey renal allograft study (Mathews et al., J. Clin. Invest. Published on Sept. 17, 2018)

- HuABC2 with belatacept (CTLA4-Ig) prolonged monkey survival much better than belatacept alone in the life-sustaining fully-MHC-mismatched renal allograft study.
- Treg ratio in CD4+ T cells did not change in peripheral blood and increased in the grafted kidney by treatment with HuABC2.
- No significant increase in CMV viremia was observed during HuABC2 treatment.