MEDICENNA
THERAPEUTICS CORP.

MDNA132: An IL-13 Superkine For Targeting IL13Rα2 Expressing Tumors

OPPORTUNITY OVERVIEW

- Medicenna is developing a pipeline of engineered cytokine products (Superkines and Empowered Cytokines), with pharmacologically-optimized receptor-binding properties.
- MDNA132 is an IL-13 cytokine variant with 16,000,000 X greater specificity towards the validated cancer antigen IL13Rα2 over the ubiquitously expressed IL13Rα1.
- MDNA132 enables improved on-tumor specificity for glioblastoma, breast cancer, colon cancer and other tumors, with the potential for reduced off-tumor side-effects.

MDNA132 is available for license for use as an attractively differentiated targeting domain for inclusion in CAR-T constructs

IL13Rα2 AS A CANCER TARGET

- IL13Rα1 is a widely expressed receptor for IL13 and IL4. IL13Rα2 is a decoy receptor for the IL-13 cytokine, that acts to dampen IL13-mediated responses in inflamed tissues.
- IL13Rα2, a cancer testis antigen, is highly expressed at the surface of certain tumor cells minimally on normal cells.
- IL13Rα2 is recognized as a major glioblastoma marker *(PMID: 18172271)* and tumor suppressor gene *(PMID:24723564)*.
- IL13Rα2 is increasingly recognized as a target and late-stage aggressiveness factor in basal-like breast *(PMID: 26208975)* and colorectal cancers *(PMID: 22505647)*.

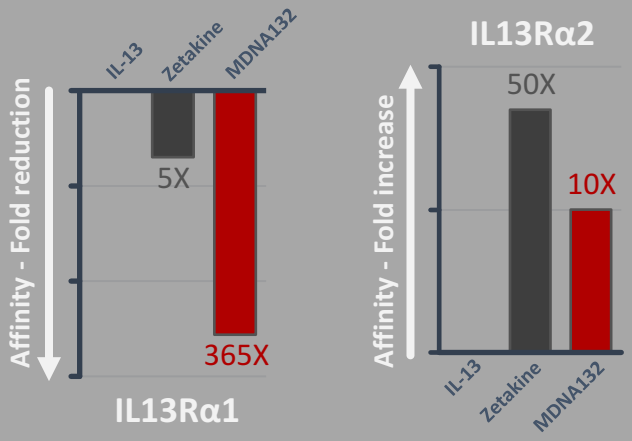
DEVELOPMENT OF MDNA132

- MDNA132 was generated from yeast display screening of a large number of mutations at key sites required for IL13 binding to IL13Rα1, IL13Rα2, and IL4Rα.
- MDNA132 has enhanced affinity for IL13Rα2 (10X lower K_D), and greatly decreased affinity towards IL13Rα1 (365X higher K_D).
- Further *in vitro* characterization of MDNA132 is ongoing.

MDNA132 has 16,000,000 X greater specificity than IL13 towards the cancer antigen IL13Rα2 vs ubiquitous IL13Rα1.

MDNA132 TO TARGET CANCER

- IL13Rα2 has been validated as a target to treat glioblastoma; an IL13-toxin fusion reaching phase III clinical trials *(PMID: 20511192)*.
- IL13Rα2 is now a targeted antigen for CAR-T cells using a mutated IL13 (zetakine, Mustang Bio), showing early signs of efficacy in phase I trials *(Brown et. Al., ASGCT meeting, May 2016)*.
- MDNA132 has superior targeting compared to IL13 and the zetakine, with lower affinity to the ubiquitously expressed IL13Rα1, while retaining sub-picomolar affinity to IL13Rα2.
- MDNA132 is a differentiated solid tumor targeting asset with solid IP.



Medicenna is planning on making this novel targeting domain available for out-license for use in immunotherapy platforms such as CARs.