IMMUNOPHERESIS®: A NOVEL IMMUNOTHERAPY PLATFORM FOR EXTRACORPOREAL REMOVAL OF SOLUBLE TARGET MOLECULES IN ONCOLOGY

Steven Josephs, Robert Segal, Steve Prince, Mathew Ong, Amir Jafri, Lawrence Florin, Victoria Manax, Michael Matho, Sameera Bilgrami, Annette Marleau*. Immunicom, Inc., San Diego, CA, USA

Background Immunopheresis® is a novel immunotherapeutic approach for treating cancer that employs Immunicom, Inc.’s proprietary technology platform for extracorporeal removal of soluble target molecules from plasma. The technology platform consists of patent-protected apheresis columns containing an affinity matrix to which customized ligands are coupled for capturing one or more cytokines, cytokine receptors and/or growth factors. The lead product, the LW-02 Column, selectively removes soluble tumor necrosis factor receptors (sTNFRs) from plasma, which are shed by tumors to neutralize TNF-α and evade its anti-tumor activities. Performance of the LW-02 Column demonstrates the effective and selective target molecule capture that is achievable using the Immunopheresis platform.

Methods The LW-02 Column comprises a trimeric single-chain TNF-α molecule covalently conjugated to an agarose bead matrix to form a proprietary high affinity resin. Laboratory performance testing of the LW-02 Column includes: 1) Capture efficiency and binding capacity for sTNF-Rs (sTNF-R1 and sTNF-R2) measured using MSD assays; 2) Leaching of ligand from the affinity matrix evaluated using MSD assays; 3) Potential off-target binding assessed by measuring plasma protein profiles and cytokine concentrations pre- and post-column exposure using HPLC and immunoassays.

Results In laboratory testing, the LW-02 Column has a capture efficiency of >80% removal of both sTNF-R1 and sTNF-R2, during recirculation of 1L test plasma through the column to model a clinical apheresis procedure. The column binding capacity exceeds the sTNF-R quantities that are typically present in cancer patients’ plasma (approximately 30 micrograms total). The quantities of TNF-α ligand that leach from the affinity matrix (equivalent to < 1 microgram per procedure) are significantly lower than TNF-α levels reported to cause clinical adverse events. The LW-02 Column exhibits selectivity for sTNF-Rs with negligible off-target binding of cytokines, immunoglobulins, or other plasma components.

Conclusions LW-02 Column Immunopheresis has a highly specific and selective mechanism of action and offers a novel subtractive therapy approach for treating cancer that avoids the typical toxicities associated with systemic drug therapy. Clinical performance of the LW-02 Column is currently being monitored as part of three ongoing clinical trials as monotherapy or as an adjunct to chemo- or immunotherapy for various solid tumors. The technology platform is being leveraged with novel high-affinity capture ligands to address other clinically relevant target molecules in immuno-oncology.