

# SCORPION<sup>™</sup> Therapeutics

The Future of Multi-Specifics

Trubion introduces a novel platform for the development of multi-specific protein therapeutics – SCORPION therapeutics. SCORPION therapeutics are single chain proteins comprised of an N-terminal binding domain, an effector domain based on immunoglobulin Fc regions, and a C-terminal binding domain, which are produced as disulfide-linked dimers by standard eukaryotic manufacturing cell lines. This proprietary molecular class leverages Trubion’s clinically proven SMIP<sup>™</sup> (Small Modular ImmunoPharmaceutical) product format by combining single-chain binding and effector domain libraries, and adding additional C-terminal binding moieties. We utilize human protein sequences selected for stability, manufacturability, spatial optimization of the binding domains, and low immunogenicity.

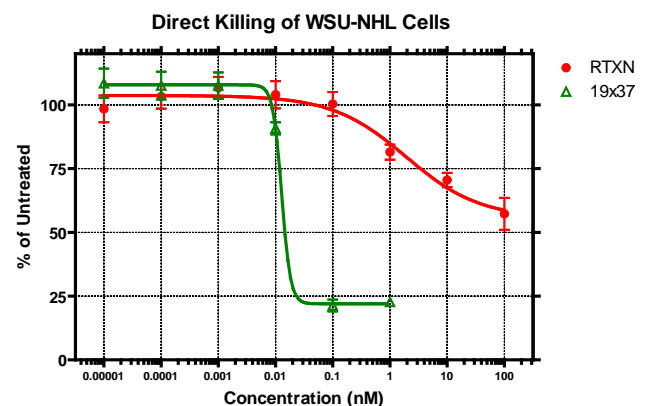
## PLATFORM OVERVIEW: SCORPION THERAPEUTICS

SCORPION therapeutics offer several important advantages:

- **Dual Targeting:** unique structure enables simultaneous multi-valent engagement of two or more different soluble or cell-surface targets, providing the capability for differentiated signaling events
- **Desirable Pharmacodynamic Properties:** retains immunoglobulin effector functions such as long *in vivo* half-life and Fc-dependent cellular cytotoxicity (FcDCC) activity, if desired
- **Rapid Development of Multiple Product Candidates:** provides for a multitude of product candidates by utilizing binding domains in a variety of target combinations
- **Reliable Manufacturing:** stable, homogeneous products with a robust manufacturing profile
- **Broad Therapeutic Application:** autoimmune and inflammatory diseases (AIID), transplant, oncology, and other high unmet need areas

## DUAL TARGETING

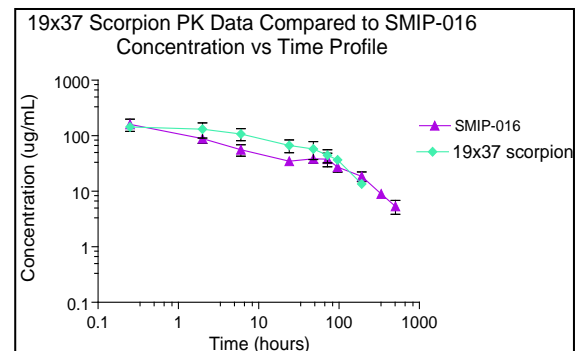
The unique structure of Trubion’s SCORPION therapeutics allows them to bind two or more different targets in a bi-valent manner with low nanomolar or sub-nanomolar affinities<sup>1</sup>. This structure also provides spacing and flexibility between the N- and C-terminal binding domains allowing SCORPION molecules to effectively cross-link cell-surface targets and drive differentiated signaling - for example, the induction of programmed cell death can be achieved in resistant malignant B-cells by cross-linking CD19 and CD37. Alternatively, SCORPION therapeutics can simultaneously bind and neutralize two soluble targets as described in our X1 SCORPION program, which targets TNF in combination with other soluble targets (e.g., IL-6/IL-6R, Tweak, TGF or RANKL).



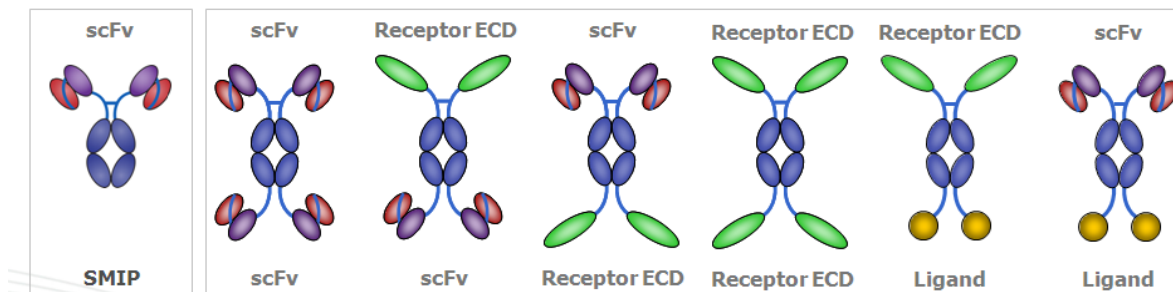
### DESIRABLE PHARMACODYNAMIC PROPERTIES

SCORPION therapeutics retain effector functions similar to SMIP and monoclonal antibody therapeutics. For example, SCORPION therapeutics, if desired, can be produced to retain potent FcDCC function. Moreover, SCORPION therapeutics plug and play with Trubion's TRU-ADhanCe™ technology, allowing FcDCC activity to be increased by over an order of magnitude, if desired.

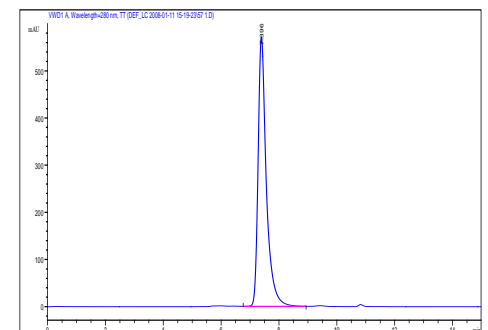
SCORPION therapeutics are serum stable with *in vivo* half-lives in circulation similar to our clinically proven SMIP therapeutics, the lead example of which, TRU-015, has a serum half-life in patients of over two weeks<sup>2</sup>. If so desired for particular therapeutic applications, SCORPION products with shorter half-lives can be readily constructed using appropriate effector domains from our effector domain library.



### RAPID DEVELOPMENT OF MULTIPLE PRODUCT CANDIDATES



SCORPION therapeutics can be rapidly developed into multiple product candidates. Development time for SCORPION therapeutics is significantly reduced by utilizing Trubion's clinically proven SMIP product format. Trubion's plug and play library components of single-chain binding domains and effector domains enable systematic optimization of therapeutics - a valuable differentiating feature compared to other therapeutic generation technologies.



### RELIABLE MANUFACTURING

SCORPION therapeutics have a robust manufacturing profile. High SCORPION expression levels in un-optimized standard eukaryotic manufacturing cell lines are consistent with production at >1gm/L upon optimization. Downstream product purification utilizes standard protein A-based strategies and yields well-characterized, homogeneous products, robust to multiple freeze-thaw cycles, which are stable for months in solution.

### **BROAD THERAPEUTIC APPLICATION**

SCORPION therapeutics have broad therapeutic application in high unmet need areas including autoimmune and inflammatory disease, solid organ transplant, oncology, and other. The autoimmune and inflammation (AIID) therapeutic market alone is greater than \$16.0B and rapidly growing with significant unmet needs in efficacy improvement, administration, and safety. The worldwide solid organ transplant rejection therapeutics market is over \$3.0B despite having limited approved therapeutic options with significant safety/tolerability issues. The worldwide oncology therapeutics market is approaching \$70.0B with an estimated 1.5M<sup>3</sup> new cases in the U.S. yearly with significant unmet needs in the majority of cancer types for improved survival, safety, and administration. Thus, the unmet needs in AIID, solid organ transplant, and oncology represent large market opportunities for SCORPION based therapeutics.

### **TRUBION ALLIANCE OPPORTUNITIES**

Trubion is in the process of constructing alliances with a select group of technology and development partners. Our alliance strategy is focused on alliances that develop Trubion product candidates for commercialization in high-value indications, or that identify and develop differentiated products against targets of mutual interest using our SMIP™, SCORPION™ and TRU-AdhanCe™ technology platforms.

### **CONTACT**

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Target	Product Candidate	Disease Indication	Development Stage				
			Design	Pre-Clinical	Phase I	Phase II	Phase III
CD20	TRU-015	Rheumatoid Arthritis (RA)	█	█	█	█	
CD20	SBI-087	Rheumatoid Arthritis (RA)	█	█	█	█	
CD20	SBI-087	Systemic Lupus Erythematosus (SLE)	█	█	█		
CD37	TRU-016	Chronic Lymphocytic Leukemia (CLL)	█	█	█		
CD37	TRU-016	Non-Hodgkin's Lymphoma (NHL)	█	█	█		
CD37	TRU-016	Autoimmune and inflammatory Disease (AIID)	█				

1. Data on file Trubion Pharmaceuticals
2. ACR 2007 PK poster
3. NCI, Cancer Facts and Figures, 2009