

Therapeutics

**INVESTIGATOR’S BROCHURE**

**[Product Name] (Product Description)**

**IND XXXXXX**

**DRAFT X.X**

**DATE dd/mmm/yyyy**

**Seattle Children’s, Seattle Children’s Therapeutics**

**CONFIDENTIAL**

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**LIST OF ABBREVIATIONS [Please edit]**

AACR American Association of Cancer Research

ALL Acute lymphoblastic leukemia

Allo-HSCT Allogeneic hematopoietic stem cell transplantation

ASH American Society of Hematology

CAR Chimeric antigen receptor

CFSE Carboxyfluorescein diacetate succinimidyl ester

CLL Chronic lymphocytic leukemia

CNS Central nervous system

CR Complete remission

CRi Complete remission with incomplete blood count recovery

CRP C-reactive protein

CRS Cytokine release syndrome

CT Computed tomography

CTCAE Common Terminology Criteria for Adverse Events

DIC Disseminated intravascular coagulation

DLBCL Diffuse large B cell lymphoma

DMSO Dimethyl sulfoxide

EEG Electroencephalogram

EGFRt Truncated human epidermal growth factor receptor

FDA Food and Drug Administration

FHCRC Fred Hutchinson Cancer Research Center

FL Follicular lymphoma

GM-CSF Granulocyte macrophage colony stimulating factor

GMP Good Manufacturing Practices

GVHD Graft versus host disease

Her2 Human Epidermal Growth Factor Receptor 2

Her2tG truncated Human Epidermal Growth Factor Receptor 2

ICU Intensive care unit

IFNγ Interferon-gamma

IL-6 Interleukin-6

IV Intravenous

mAb Monoclonal antibody

MAS Macrophage activation syndrome

MCL Mantle cell lymphoma

MMSE Mini Mental State Examination

MRD Minimal residual disease

MRI Magnetic resonance imaging

MSKCC Memorial Sloan Kettering Cancer Center

MRD Minimal residual disease

MTD Maximal tolerated dose

NCI National Cancer Institute

NHL Non-Hodgkin lymphoma

NSG NOD/Scid IL-2RCnull

PBMC Peripheral blood mononuclear cell

PK Pharmacokinetic

RCL Replication-competent lentivirus

R/R Relapsed or refractory

scFv Single chain variable fragment

SCID-X X-linked severe combined immunodeficiency

SCRI Seattle Children’s Research Institute

sCRS Severe cytokine release syndrome

SCTx Seattle Children’s Therapeutics

TNFα Tumor necrosis factor-α

TLS Tumor lysis syndrome

# SUMMARY

[Provide a general background of the indication, previous experience and rationale for developing the investigational product].

# INTRODUCTION

## 2.1 [Description of Indication]

## 2.2 [Specific antigen] presence in the indication

 [Provide a rationale]

## 2.3 [Specific Antigen] as a Therapeutic Target

[Provide background and rationale]

## 2.4 [Specific Antigen]-Targeted Chimeric Antigen Receptors

## 2.5 Previous *in vivo* Human Experience with {Investigational Product]

[Provide a short summary of previous human experience with the investigational product or similar product].

## 2.6 Investigational Drug Product: [Product name]

{A short description of the investigational product].

# PHYSICAL, CHEMICAL, AND PHARMACEUTICAL PROPERTIES AND FORMULATION

A description of the [Investigational cell product] components, product tracking, packaging, labeling, storage and handling instructions will be provided to each clinical site with on-site training conducted and documented by SCTx personnel.

## 3.1 [Investigational Product] Manufacturing Process

[Provide a short summary of manufacturing process. Usually TCPC provides this summary].

See Figure 1 for an overview of the manufacturing process.

Figure 1: [Product Name] Manufacturing Process

[Insert Product Manufacturing diagram]

## 3.2 [Investigational Product] Cell Thawing, Preparation and Administration

Detailed procedures for cell product receipt, thawing, preparation, and administration will be provided to each clinical site with on-site training conducted and documented by SCTx personnel.

# NONCLINICAL EXPERIENCE

## 4.**1 Summary of Pharmacology Studies**

### 4.1.1 Summary of *In Vitro* Studies

[Insert in vitro study summary]

4.1.2 Summary of *In Vivo* Studies

[Insert in vivo study summary]

4.1.3 Summary of Efficacy

[Insert in vitro or in vivo efficacy data]

4.1.4 Marketing Experience

# EFFECTS IN HUMANS

[Insert summary of effects in humans. If first-in-human product, then insert summary of related products in humans.]

# GUIDANCE FOR INVESTIGATORS

## 6.1 Summary of Potential Risks and Management of Toxicities

## [Some common CAR T cell related toxicities are listed below as examples, you may have to revise the list as per your CAR T Cell product]

### 6.1.1 Cytokine Release Syndrome

### 6.1.2 Fever

### 6.1.3 Neurologic Toxicities

### 6.1.4 Macrophage Activation Syndrome

### 6.1.5 T Cell Infusion Reactions

### 6.1.6 Tumor Lysis Syndrome

### 6.1.7 B cell Aplasia

### 6.1.8 GVHD

### 6.1.9 Uncontrolled T cell Proliferation

### 6.1.10 Replication-Competent Lentivirus, Clonality, and Insertional Oncogenesis

## 6.2 Regulatory Reporting:

[Description of any previously observed Toxicities of this product]

# REFERENCES

[List of references]

# Appendices [if any]