Clinical Development of an N-cadherin Antibody to Target Cancer Stem Cells

Grant Award Details

Clinical Development of an N-cadherin Antibody to Target Cancer Stem Cells

Grant Type: Early Translational IV

Grant Number: TR4-06867

Project Objective: The goal of this Development Candidate project is to identify a human or humanized antibody targeting N-cadherin as a potential therapy to target castration-resistant prostate cancer and prostate cancer stem cells.

The **Goal** of the Amended activities is to get to a state of readiness to be able to apply for a CIRM CLIN1 grant [The goal of a CLIN1 award is to file an IND with 18-mo; activities supported under CLIN1 could include production of GLP material as well as the conduct IND-enabling studies]. **Activities** to be conducted include:

Generate a GMP-compatible pooled/clonal production cell line for the Lead HuMab
Success criteria: line meets regulatory requirements
Line could support the production of gram quantities of HuMab sufficient to conduct GLP safety studies and a Phase 1 trial
Produce sufficient research-grade MAb to conduct pilot PK and Tox studies
Demonstrate that NHP is a relevant Tox species:
Binding to cells/target protein
Biological activity in vitro
Tissue cross reactivity (non-GLP study)
Develop and qualify/validate a NHP PK assay to support the pilot studies – *suggest outsourcing this*
Conduct pilot PK study in NHP (by end of month 12)
Conduct pilot acute Tox study in NHP (by end of month 12)
Sample design:
2-week study
3 dose levels (low, med, high) plus placebo
small number of animals
Complete cell line development so as to be ready for cell banking

Investigator:

Name:	Robert Reiter
Institution:	University of California, Los Angeles
Type:	PI

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Name:	Anna Wu
Institution:	University of California, Los Angeles
Type:	Co-PI

Disease Focus: Cancer, Prostate Cancer, Solid Tumors

Human Stem Cell Use: Cancer Stem Cell

Award Value: $4,075,668

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: OM#2

View Report

Grant Application Details

Application Title: Clinical Development of an N-cadherin Antibody to Target Cancer Stem Cells

Public Abstract:	Metastatic disease and the castration resistance remain tremendous challenges in the treatment of prostate cancer. New targeted treatments, such as the ant-testosterone medication enzalutamide, have improved the survival of men with advanced disease, but a majority develops treatment resistance. The field of cancer stem cells hypothesizes that treatment resistance emerges because stem cells are inherently resistant to our current therapies and eventually repopulate tumors. One mechanism by which cancer stem cells resist therapy is through acquisition of an epithelial to mesenchymal transition (EMT), a phenomenon of normal development used by cancers to survive and metastasize. Our laboratory has shown that prostate cancers undergo an EMT that leads to invasion, metastasis and treatment resistance. N-cadherin, a critical regulator of EMT, is expressed in most castration resistant prostate cancers (CRPC) and is sufficient to promote treatment resistance. We therefore developed antibodies against N-cadherin, which are able to inhibit growth, metastasis and progression of prostate cancers in vivo. The goal of this translational application is to move this promising treatment from the laboratory to the clinic by making the antibody human, making it bind more strongly, and then testing it for toxicity, behavior and anti-tumor activity. At the completion of this project, we will be poised to manufacture this lead molecule and move expeditiously to Phase I clinical studies.
Statement of Benefit to California:	Prostate cancer is the second leading cause of cancer-related death in Californian men. With an aging population, this problem is expected to continue to grow despite recent advances in treatment. The goal of this application is to develop a novel antibody targeting a cancer stem cell target in hormone and treatment refractory prostate cancer. The benefit to the California, if successful, will be the development of a novel therapy against this common disease.