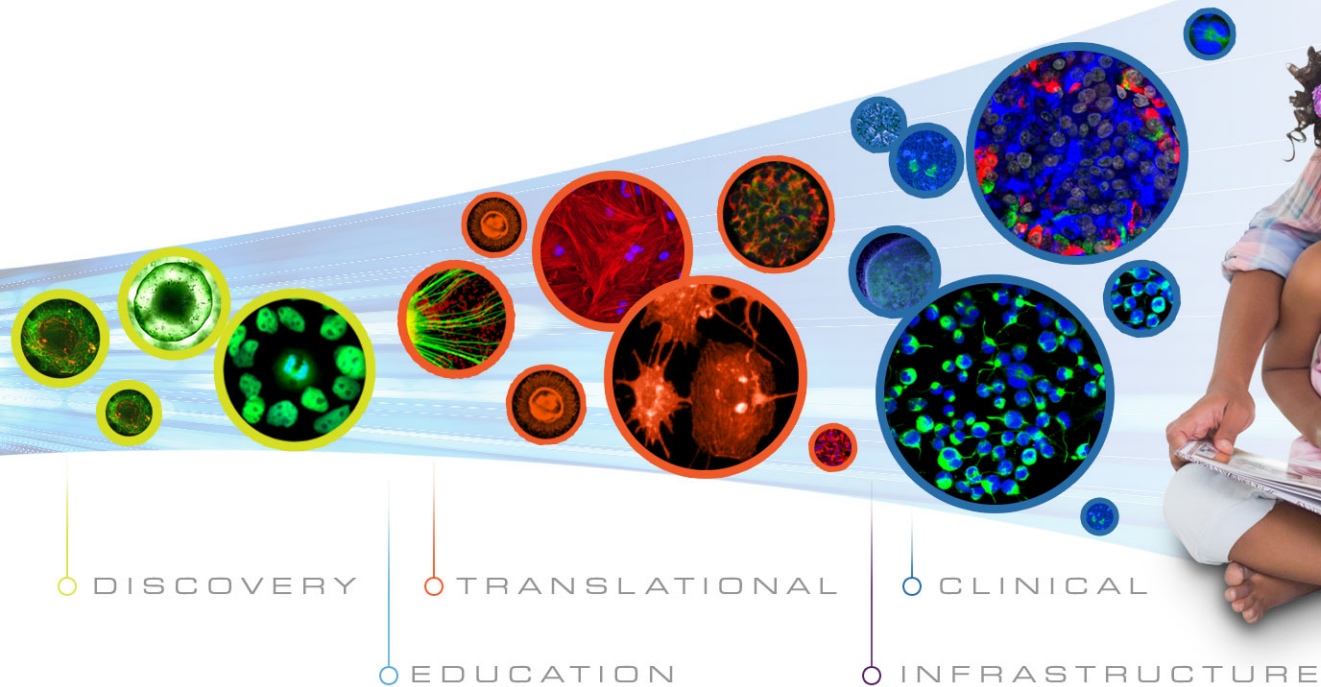


# CIRM

CALIFORNIA'S STEM CELL AGENCY

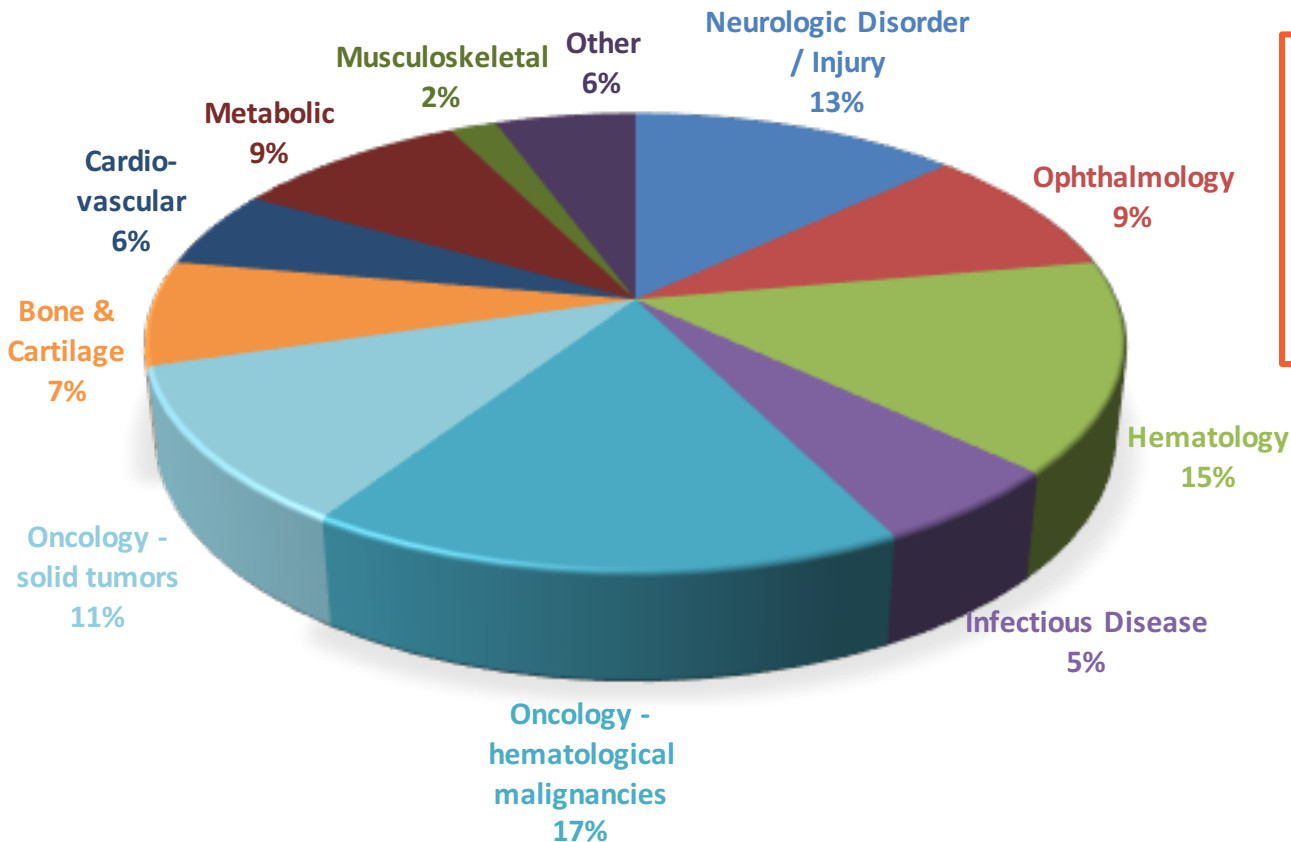


## Clinical Program Review: Oncology

Ingrid Caras, Ph.D.

Associate Director, Therapeutics  
California Institute for Regenerative Medicine

# Diverse Clinical Stage Portfolio

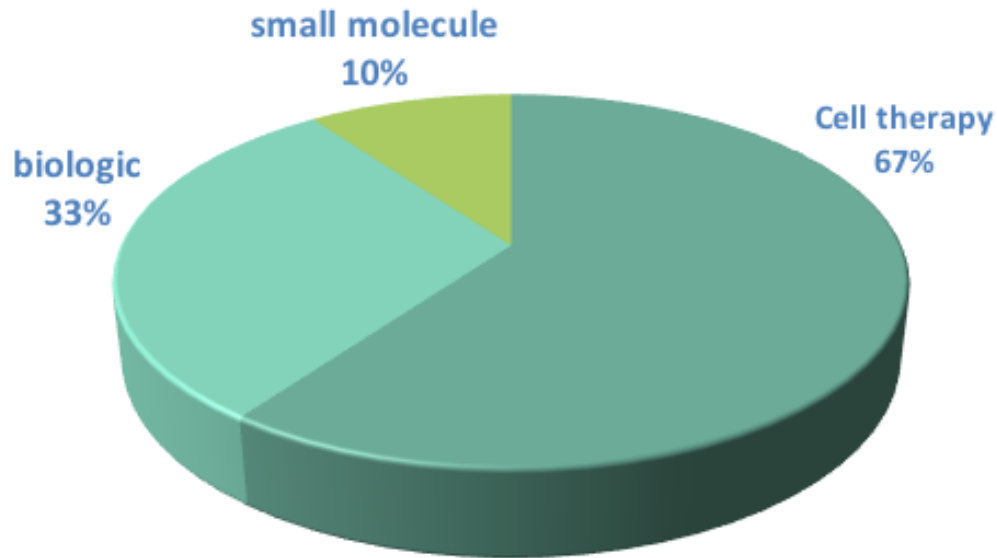


43 Clinical Trials  
(38 active)

8 Preparing IND

# 10 Active Oncology Clinical Trials

# Oncology Clinical Trials



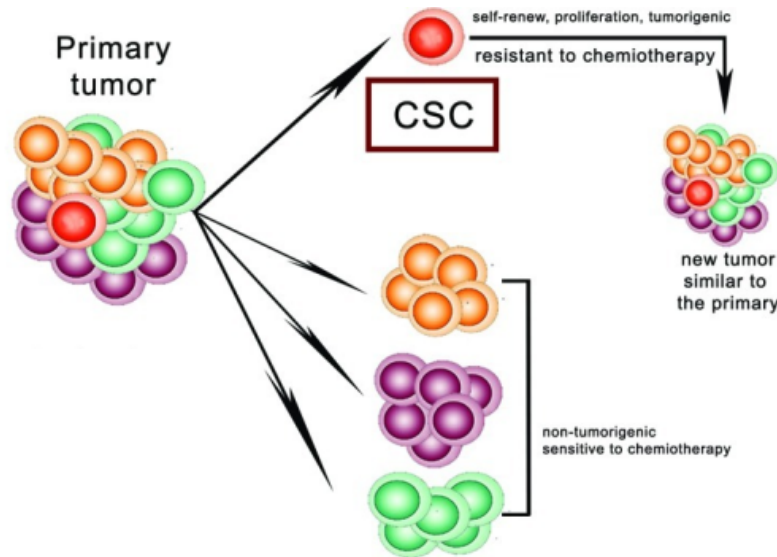
## Therapeutic Modality

6 Cell Therapy

3 Biologic

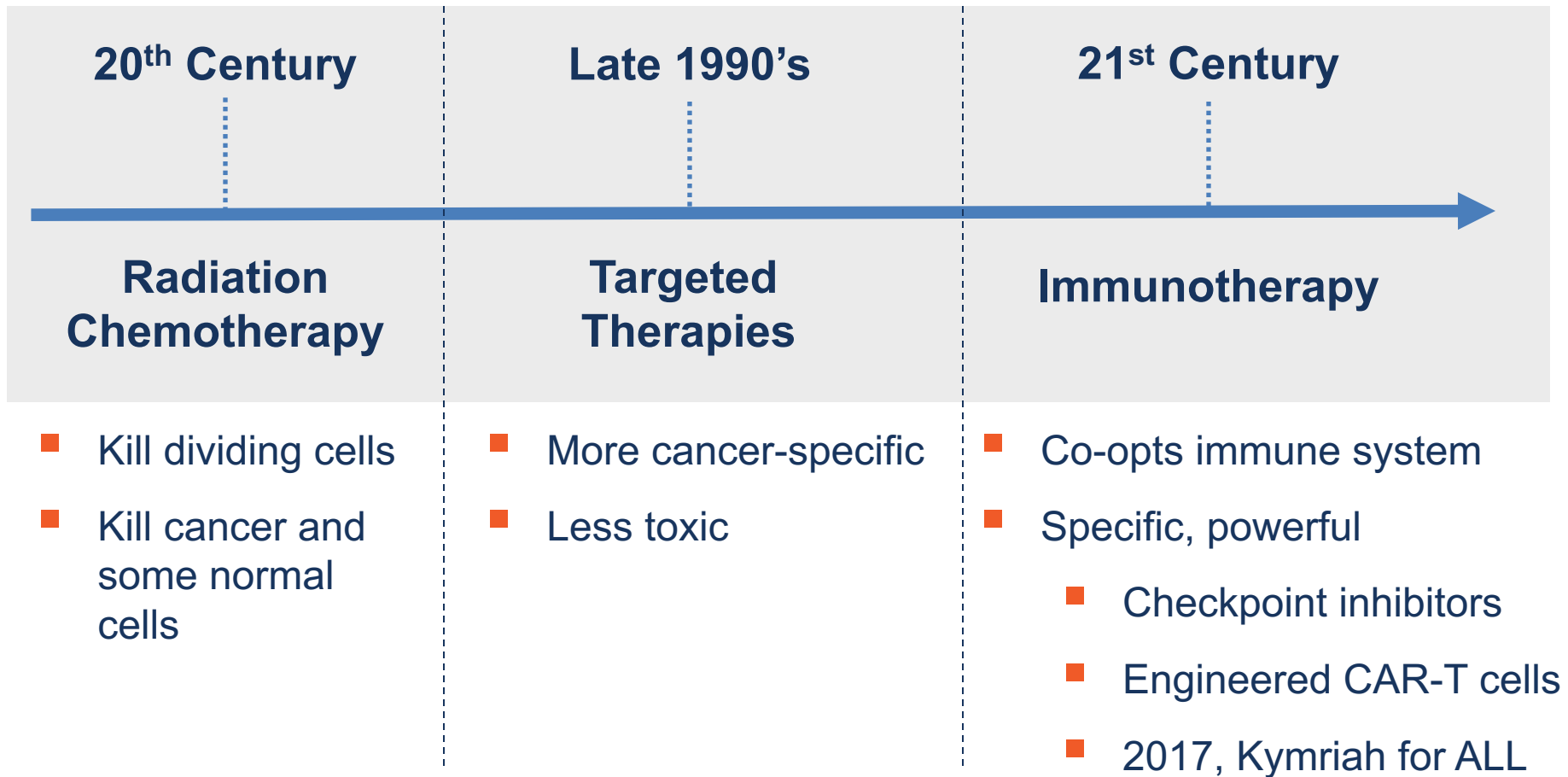
1 Small Molecule

# Cancer Stem Cell Concept



- Tumor growth is fueled by small numbers of self-renewing CSC
- CSC are resistant to radiation and chemotherapy and can re-grow the tumor and drive relapse after remission
- Explains why tumors recur after initially successful therapy
- CSC can spread to distant sites and drive metastases
- **CSC must be eradicated to achieve a cure**

# Evolution of Cancer Treatment



# Active Clinical Trials

## Hematological Malignancies

Indication	Investigator / Organization	Phase	Status	Targeted Enrollment
Multiple Myeloma	Spear/Poseida	Phase 1	Enrolling	40
Acute myeloid leukemia	Chao/Forty Seven Inc.	Phase 1b	Enrolling	96
Chronic lymphocytic leukemia	Kipps/UCSD	Phase 1b/2a	Enrolling	56
Hematologic malignancies	Finnegan/Angiocrine	Phase 1	Initiating	12
Acute myeloid leukemia	Delaney/Nohla	Phase 2	Initiating	220
Immunosuppressed patients with persistent viral infections	Pulsipher/CHLA	Phase 1/2	Initiating	60

# Active Clinical Trials

## Solid Tumors

Indication	Investigator / Organization	Phase	Status	Targeted Enrollment
Malignant Glioma	Brown/COH	Phase 1	Enrolling	100
Synovial Sarcoma and Advanced tumors	Ribas/UCLA	Phase 1	Initiating	12
Colorectal cancer and solid tumors	Chao/Forty Seven Inc.	Phase 1b/2a	Enrolling	112
Solid Tumors	Slamon/UCLA	Phase 1	Enrolling	84



# Immunotherapy: CAR-T for Malignant Glioma

## Investigator:

Christine Brown, M.D.

## Institution:

City of Hope



## Rationale

- Malignant glioma is a highly lethal disease with low survival rates
- Engineered CAR-T-cells are a promising strategy to treat cancer
- Developed a CAR-T cell therapy targeting IL-13 receptor alpha 2 (IL13R $\alpha$ 2) expressed on malignant glioma cells
- CAR-T cell persistence is critical for durable effect
- Use *stem cell memory T-cells* which have stem cell-like properties i.e. self-renew and differentiate – drive long-term persistence
- Progression from earlier CIRM grant

## Goal and Design

- Phase 1 trial of stem cell memory CAR-T cells targeting IL13R $\alpha$ 2 for patients with malignant glioma
- Objectives: Safety and Efficacy, Route of delivery and Dose

## Status

- Enrolling patients

# Immunotherapy CAR-T for Multiple Myeloma

## Investigator:

Matthew Spear, M.D.

## Institution:

Poseida Therapeutics



## Rationale

- Multiple myeloma (MM) is an incurable and ultimately fatal disease
- BCMA (B-Cell Maturation Antigen) expressed on MM cells is an attractive target for a CAR-T approach
- Using autologous *stem cell memory T-cells* designed to increase T-cell persistence

## Goal and Design

- Phase 1 FIH clinical trial of stem cell memory CAR-T cells targeting BCMA
- Objectives: Safety and Efficacy

## Status

- Initiating trial

# Immunotherapy: TCR for Synovial Sarcoma

## Investigator:

Antoni Ribas, M.D.

## Institution:

UCLA



## Rationale

- NY-ESO-1 is a tumor antigen expressed in many advanced cancers including synovial sarcomas
- T-cells engineered to target NY-ESO-1 have shown remarkable antitumor efficacy BUT the T-cells don't persist and patients relapse
- Approach: engineer both T-cells *and* stem cells and co-administer
- T-cells provide immediate effect while engrafted stem cells will provide a renewable source of engineered T-cells

## Goal and Design

- Phase 1 clinical trial of dual cell therapy combining stem cells and T-cells engineered with an NY-ESO-1 TCR
- Objectives: Safety, Feasibility, Efficacy

## Status

- Initiating trial

# CD47 Blockade: Novel Immunotherapy Approach



Macrophage engulfing a cancer cell

- CD47 is over-expressed on cancer and csc and is an important mechanism for immune evasion from macrophages
- CD47 blockade takes the brakes off macrophages and enables them to eliminate cancer and csc
- CD47 blockade is a novel **Immunotherapy** approach with broad applications spanning multiple tumor types

# CD47 Blockade Development History

## Preclinical Evidence for csc-targeting

- CD47 blockade prevents transfer of human AML by eliminating csc
- CD47 blockade prevents tumor growth and metastasis of solid cancers in mice

### Investigator:

Mark Chao, MD, PhD

### Company:

Forty Seven Inc.



2 Active CIRM2.0  
CLIN2 Trials

2010

Disease Team 1

Research Concept → IND

2014

Disease Team 3

Phase 1  
solid tumor trial in US  
AML trial in UK



Phase 1b in AML

- High-risk patients
- Combo with chemotherapy

Phase 1b/2a Colorectal Cancer

- Combination with cetuximab

# CSC-Targeted Therapies

**Investigator:**

Thomas Kipps, MD, PhD

**Institution:**

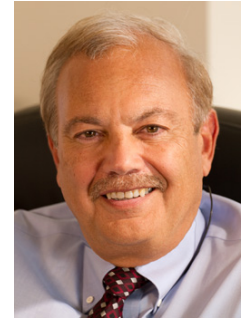
UCSD/Oncternal

**Investigator:**

Dennis Slamon, MD

**Institution:**

UCLA

**Rationale**

- Biologic or small molecule targeting pathways important for csc
- Prevent transfer and propagation of human cancers in mice by eliminating csc
- Progressions from DT1 and DT3

**Goal and Design**

- Kipps: Phase 1b/2a trial in CLL testing cirmtuzumab in combination with ibrutinib
- Slamon: Phase 1 trial in advanced solid tumors

**Status**

- Initiating/in progress

# Cord Blood Expansion Cell Therapies

**Investigator:**

Colleen Delaney, M.D.  
MSc

**Institution:**

Nohla Therapeutics

**Investigator:**

Paul Finnegan, M.D.,  
M.B.A.

**Institution:**

Angiocrine Bioscience

**Rationale**

- Cord blood expansion cell therapies –stem and progenitor cells
- Designed to improve/provide immune reconstitution after high-dose chemotherapy

**Goal and Design**

- Nohla: Phase 2 clinical trial in AML patients
- Angiocrine: Phase 1 trial in hematological cancers

**Status**

- Initiating trial

# Oncology Clinical Trials Summary

- Diverse oncology portfolio
- Majority cell therapies
- Cutting edge immunotherapy approaches
- Cancer-stem cell targeted therapies
- Programs funded by CIRM from inception



# COURAGEOUS

A close-up portrait of an elderly man with white hair, glasses, and a mustache, smiling warmly. He is wearing a blue and white patterned shirt. The background is a solid dark blue.

Karl Trede

Diagnosed with throat  
cancer, then later lung  
cancer, for which there  
was no effective  
treatment

Every Moment  
Counts

**CIRM**  
CALIFORNIA'S STEM CELL AGENCY