

Dissemination of CAR T Trials-Platforms and Partnerships

Cellicon Valley '21: The future of cell and gene therapies

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DISCLOSURES

Lentigen/Miltenyi: CARs (Patents/IP): mesothelin, dual CD19/CD20
huCD19, huCD22, huCD20, huCD33, huCD123, huCD38, huCD138, huROR1
Licensed TSLPR (NIH), CAR combinations (DuoCARs, HIV), rapid TCR cloning
Research Support

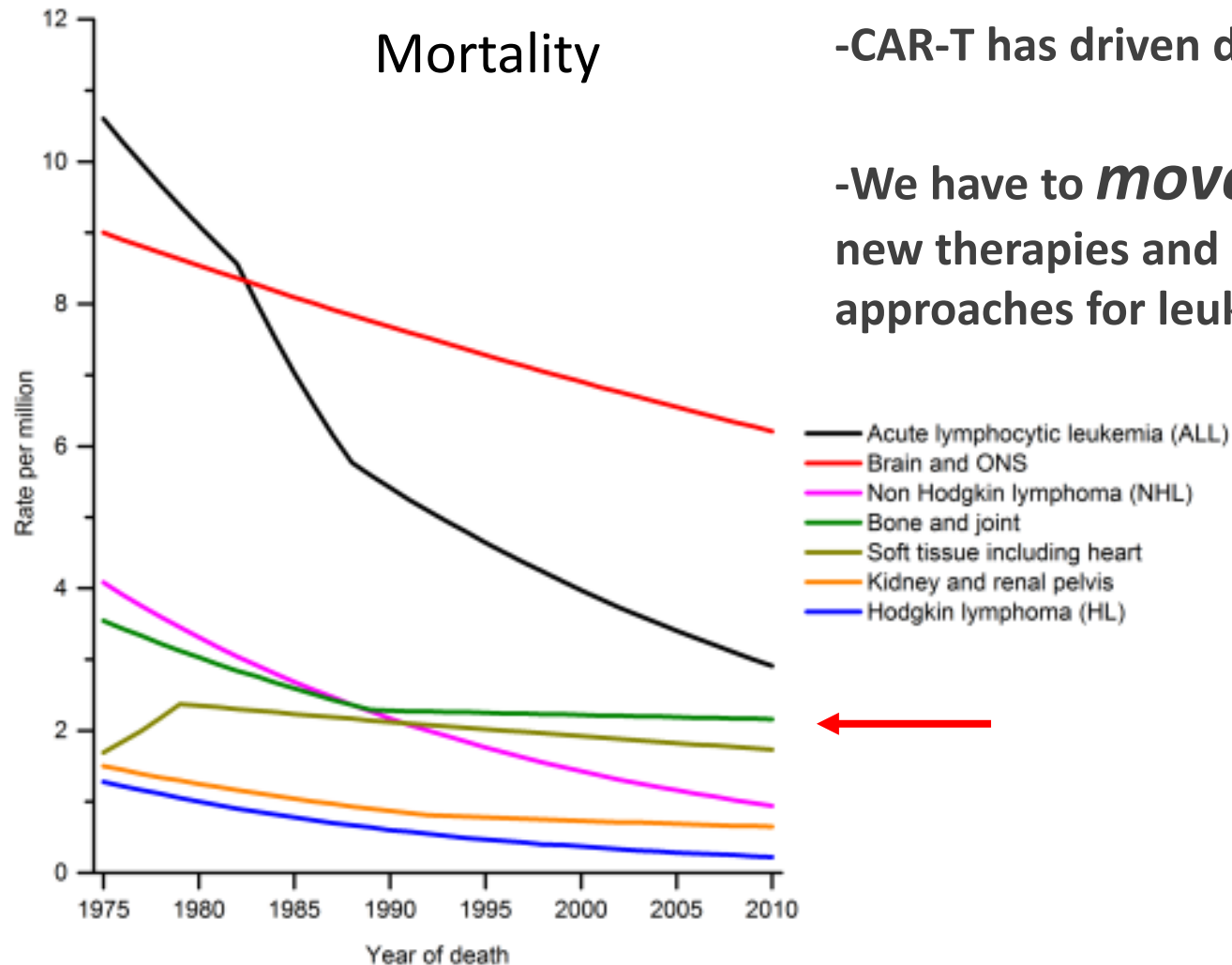
Umoja Biopharma: Consulting

USA, DHHS/NIH: CARs (Patents/IP) : CD22 (general), CD22 (m971), CD19-CD22 tandem,
ALK, B7H3 (CD276), FGFR4

SCRI: CARs (Patents/IP): FGFR4, IL1RAP

In Pediatrics, there has been no significant improvement in *decades* for soft tissue and bone tumors.

Ward et al, 2014,
CA Cancer J Clin



-CAR-T has driven down leukemia mortality

-We have to ***move faster*** to develop new new therapies and refine existing CAR-T approaches for leukemia



To support internal programs, and to share protocols with a set of like-minded academic institutions the Immunotherapy Integration Hub and subsequently the CureWorks Initiative were established

Why

To pioneer cancer immunotherapies for childhood cancers capable of disease eradication with limited sequelae that diminish the QOL of survivors

How

By integrating the entire enterprise to maximize institutional capabilities and accelerate the tempo of progress

What

A hub for Cancer Immunotherapy/CAR T-Cell translational research enterprise – from pre-clinical development through IND supported clinical trial conduct



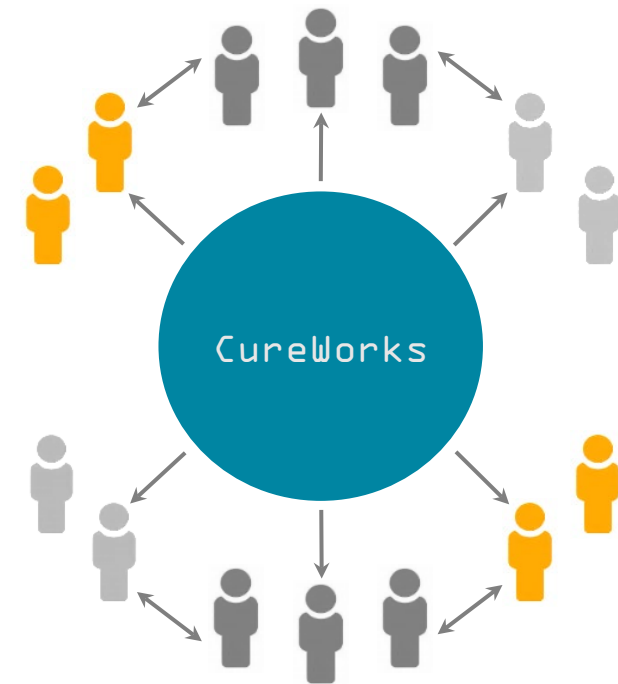
Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION



CureWorks
A NEW WAY TO BETTER CURES

CureWorks Model

- Member organizations will participate in CureWorks through a formal Agreement
- The CureWorks is an independent federation of stakeholder children's hospitals performing collaborative clinical trials in immuno-oncology
- Members pay dues and self-govern through an advisory committee
- Dr. Jensen serves as executive director

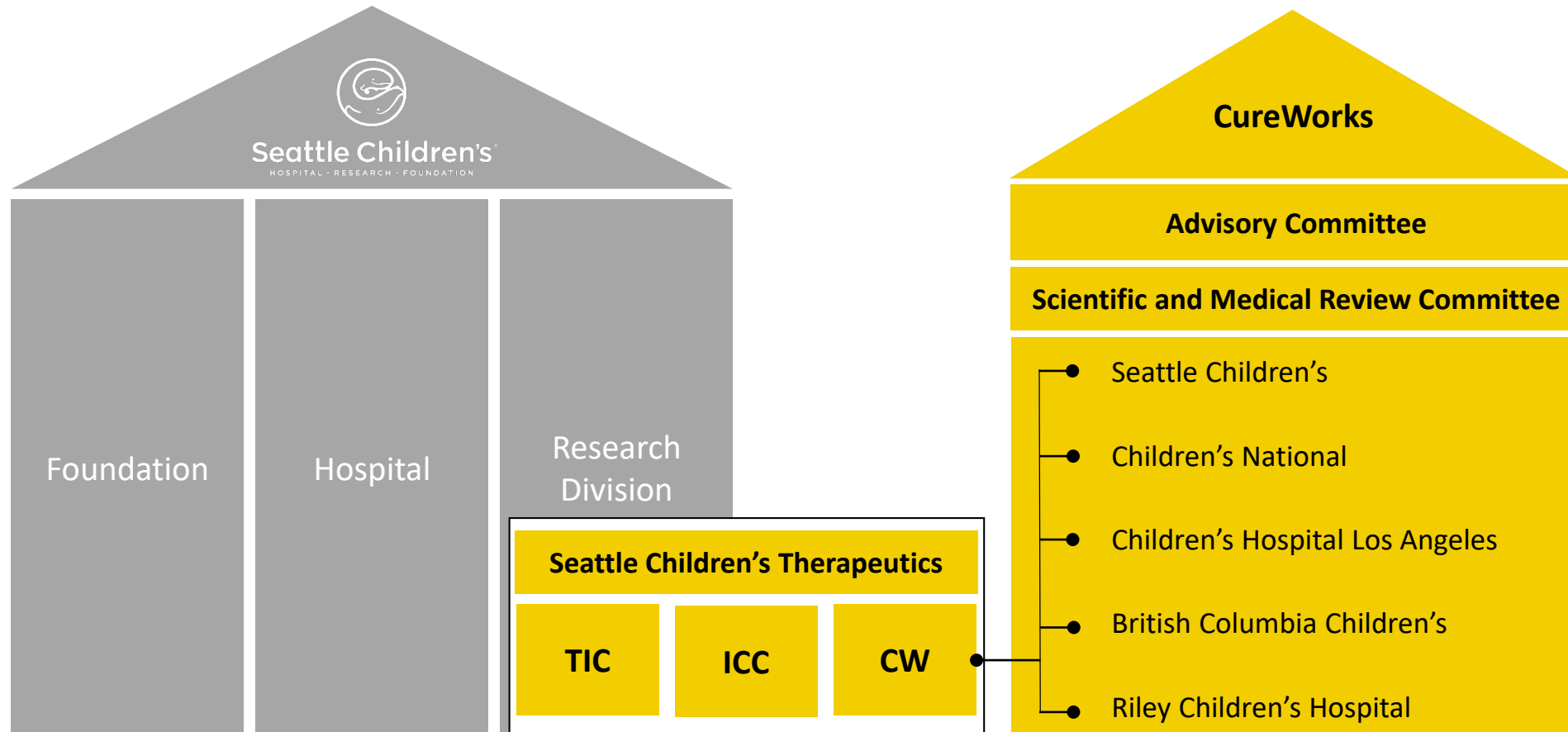


CureWorks Member Benefits

- Accelerating translation from bench to bedside
- More efficient development of IND products
- Access to GMP manufacturing
- Process development
- Clinical trial management
- Regulatory affairs support
- More diversity of patients and clinical data
- Collaborative and competitive grant proposals



Immunotherapy Enterprise Extends Beyond Seattle Children's



TIC – Therapeutics Innovation Core ICC – Immunotherapy Coordinating Center CW – CureWorks

Capabilities with Seattle Children's and the CW Cooperative

Seattle Children's Therapeutics			Seattle Children's
Therapeutics Innovation Core	Coordinating Center	CureWorks	Therapeutic Cell Production Core
R&D	Clinical Trials Management	Operations	Product Manufacturing
Process Development	Biostatistics	Marketing and Communications	Product QC Release Testing
Assay Development	Data Management	Trial Design & Conduct Consultation	Cell Banking
Correlative Studies Core	Regulatory	Trial Logistics	Stability Testing Program
			Member Funds
			Fee for Service
			Internal Program

An Integrated Approach to Immunotherapy

The Immunotherapy team has worked collaboratively across the enterprise to approach this program in an integrated manner



- **Integration Challenges**
- Accurately predicting trial enrollment and patient volumes
- Adjusting clinical services to accommodate clinical trial enrollment predictions
- Proactive hiring and training of staff
- Predicting internal and external product demand
- Prioritizing SCH enrollment while implementing a multi-site trial strategy

CureWorks Value Proposition

Seattle Children's

- Impact on survival and QOL in pediatric oncology
- Leverage existing & continued investments
- GMP investment offset by revenue from CureWorks Members
- Increased hospital revenues
- Provides national/International recognition
- Halo effect for broader revenue opportunities (grants, contracts, philanthropy)

Member Hospitals

- Ability to treat research patients locally
- De-risks and decreases investment
- Immediate access to unique technologies, expertise & data
- Increased hospital revenues
- Regional strength for accrual of subjects
- Potential for broader revenue opportunities (grants, contracts, philanthropy)

CureWorks removes the complexities of building equivalent capabilities and leverages technologies for Seattle Children's and Member organizations

Building Cure Enables High-Capacity Processing



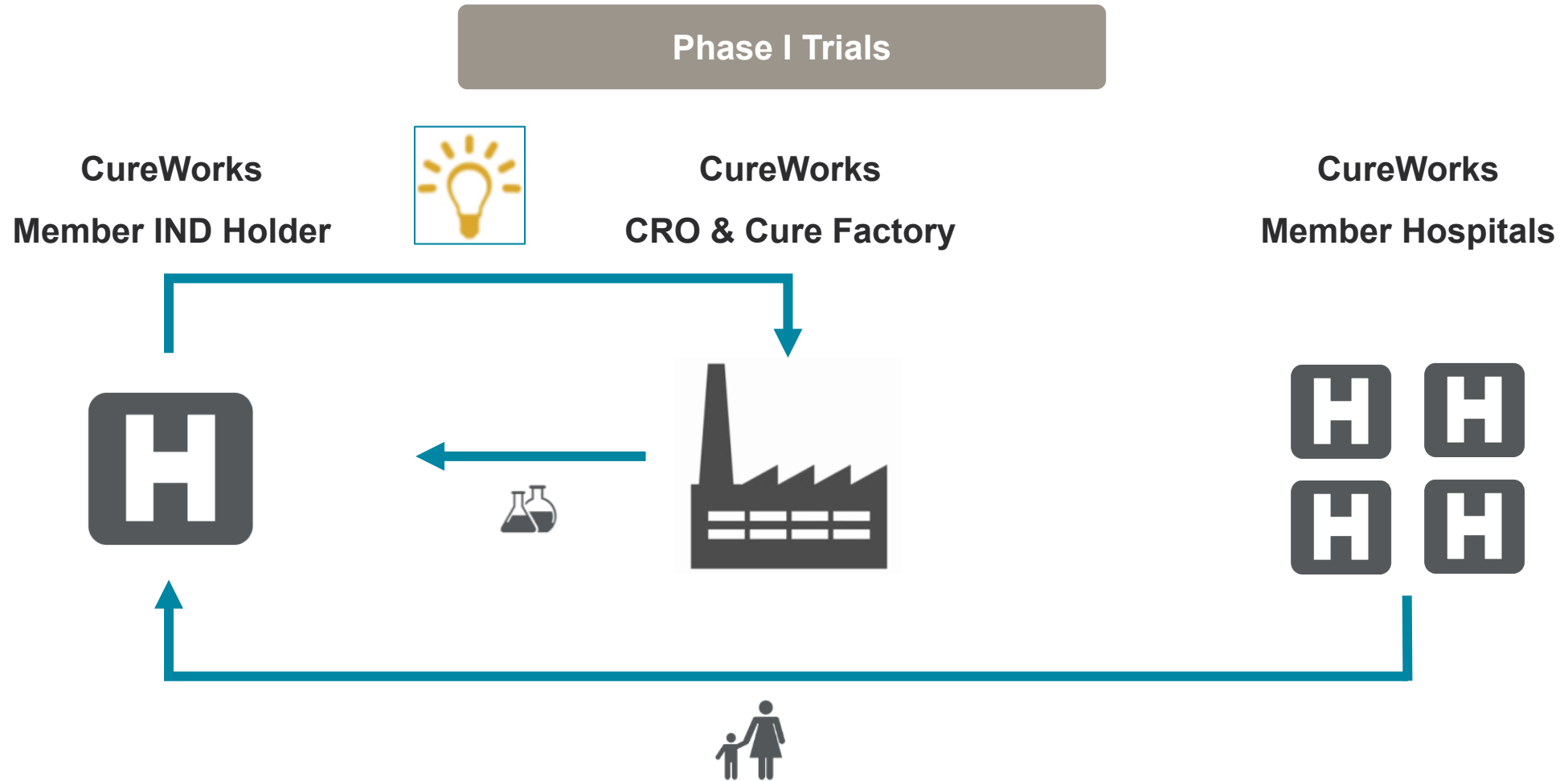
High-Capacity
Processing
Suite 1 and
Incubator Farm



Final Product
Vialing Suite

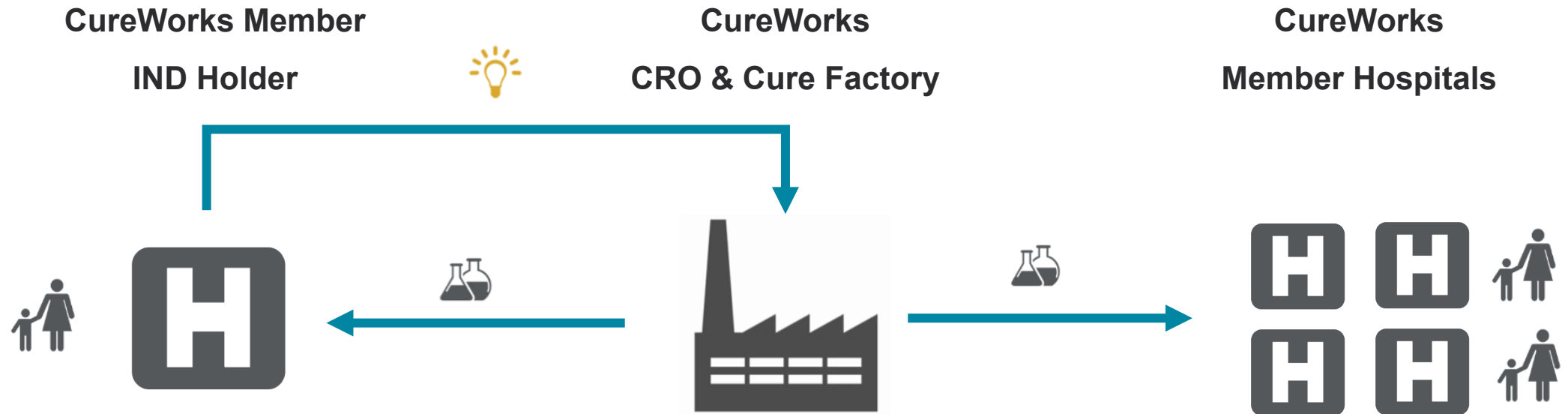
High-Capacity
Processing Suite 2
and Incubator
Farm

Treatment & Patient Flow



Treatment & Patient Flow

Phase II/III Trials



Pediatric Cancer CAR T Cell – SCRI Clinical Trial Pipeline

Immunotherapy Clinical Trials Pipeline				
Trial	Phase	O	N	D
PLAT-02	P2			
PLAT-03	P1			
PLAT-04	P1			
PLAT-05	P1			
PLAT-06	P2			
PLAT-07	P3			
ENCIT-01	P1			
BrainChild-01	P1			
BrainChild-02	P1			
BrainChild-03	P1			
BrainChild-04	P1			
STRIVE-01	P1			
STRIVE-02	P1			
STRIVE-03	P2			
ENDOCYTE	P1			

PLAT - Pediatric Leukemia Adoptive Therapy

- PLAT-02: muCD19CAR T Cell
- PLAT-03: CD19CAR T Cells + CD19t + T-APC's
- PLAT-04: CD22CAR T Cells for CD19neg Antigen Escape ALL
- PLAT-05: CD19x22 Bispecific T cells
- PLAT-06: huCD19CAR T Cell

ENCIT - Engineered Neuroblastoma CAR Immunotherapy

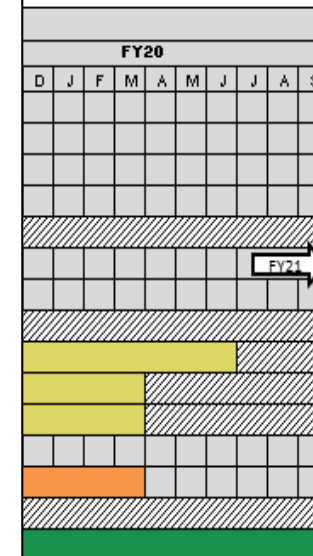
- ENCIT-01: L1CAM CAR G2 vs G3

BrainChild - Locoregional CAR T Cell Immunotherapy for Pediatric Brain Tumors

- BrainChild-01: HER2CAR T Cells
- BrainChild-02: EGFRCAR T Cells
- BrainChild-03: B7H3CAR T Cells
- BrainChild-04: IL13Ra2CAR T Cells

STRIVE - Solid Tumor Immunotherapy

- STRIVE-01: EGFR806 basket trial
- STRIVE-02: B7H3CAR basket trial



The background of the entire image shows the silhouettes of three children, two girls and one boy, standing against a bright, hazy sunset sky. They are all reaching up and holding large puzzle pieces. The puzzle pieces they are holding, along with others visible in the air, form the shape of a person. The overall mood is hopeful and aspirational.

Imagine a World Without Disease

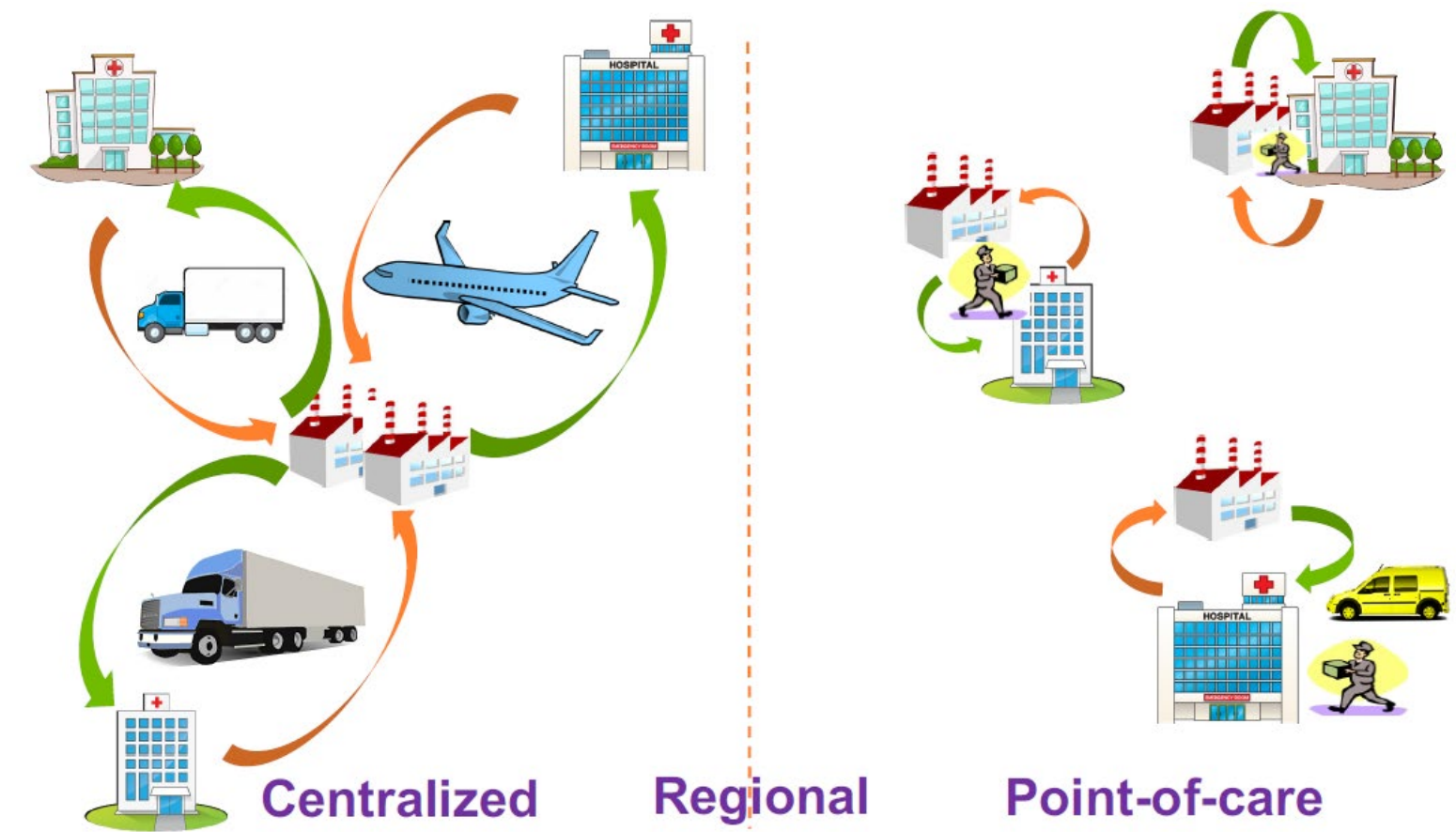
Advanced medicines are curing disease
Let's make them affordable and accessible



CaringCross

caringcross.org

Do CAR T Cells Need To Be a Commercial Pharmaceutical Product?
Do we have time to wait for Pharma to develop each product when patients could benefit now?
Can a CAR-T program benefit Hospitals/Medical Schools/Cancer Centers, both financially and intellectually?



CAR-T cells are producing amazing clinical results in patients with leukemia and lymphoma - when manufactured locally at hospitals

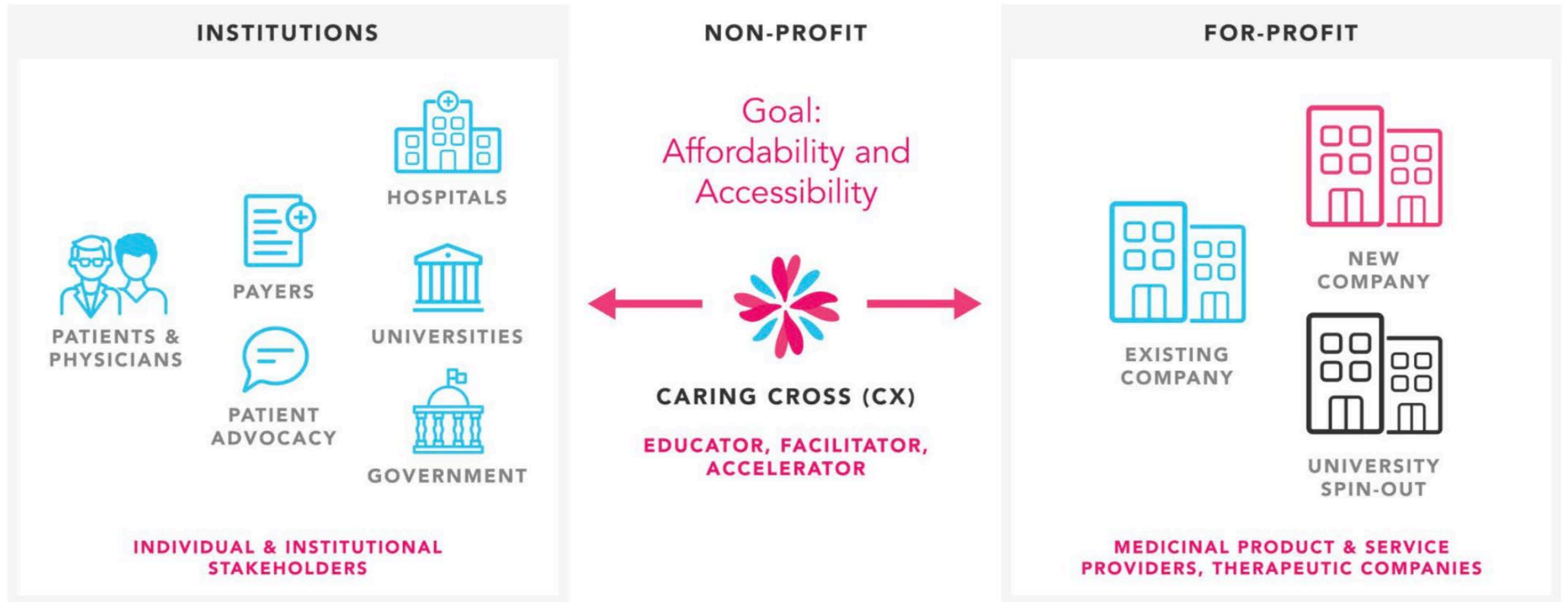


Remarkable results compared to drugs or transplantation at ~35%

CR, complete response; PR, partial response; ORR, overall response rate

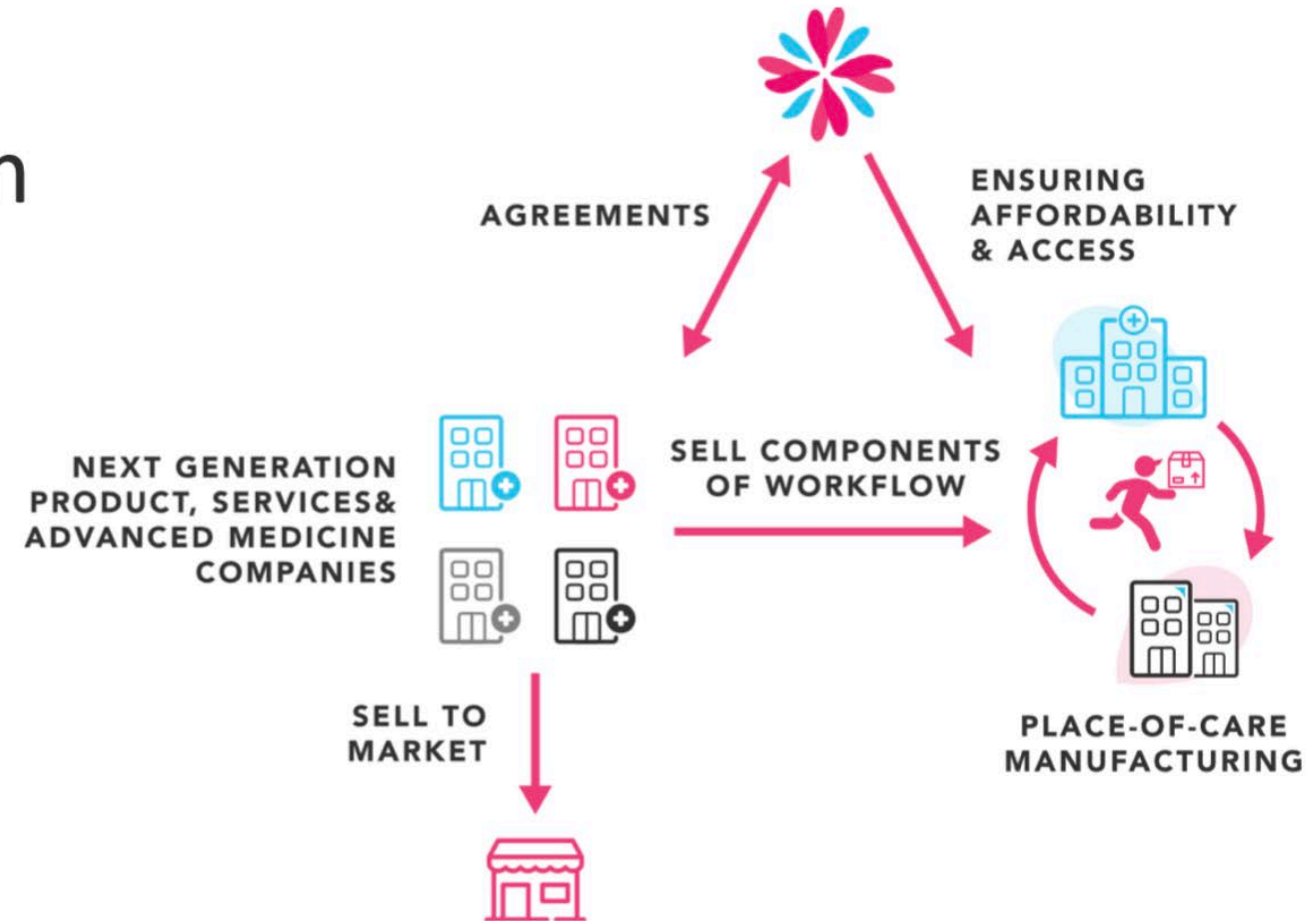
1. Case Western Reserve University (CWRU)
 - 14 out of 17 patients had a **CR or PR** - 82% ORR
 - Low toxicity compared to current CAR-T therapy
2. Dimitry Rogachev National Research Center in Moscow, Russian Federation
 - 19 out of 21 patients had a **CR or PR** – 90% ORR
 - Low toxicity compared to current CAR-T therapy
3. Medical College of Wisconsin
 - 12 out of 12 patients had a **CR or PR** – 100% ORR
 - Low toxicity compared to current CAR-T therapy

How will Caring Cross help reduce cost & improve access of innovative medicines?



Enabling Next Generation of Products, Services and Medicines with an Ecosystem of Impactful Companies

Given the success of genetic medicines, each company has tremendous potential to create impact for society and value for investors. These companies are linked by charters and agreements to ensure affordable and accessible advanced medicines.



Participating organizations with diverse capabilities=Partnerships!

Formation of the Global Gene Therapy Initiative



Joint Clinical Research Centre
Kampala, Uganda



Christian Medical College
Vellore, India



GEORGETOWN UNIVERSITY
Georgetown University Medical Center

Uganda bears a disproportionate disease burden in SCD and HIV, as does India in β -Thalassemia

Estimates of amounts (and prevalence) by geography and disease:

World

- SCD: 300 million (4%) with trait
20 million (0.3%) with disease¹²
- β -Thalassemia: 120 million (1.5%) with trait³
70,000 / year born symptomatic⁴
- HIV: 38 million (0.8% among adults)⁵



Uganda

- SCD: 6 million (13.3%) with trait
300,000 (0.7%) with disease⁶²
- β -Thalassemia: Unclear
- HIV: 1.5 million (5.8% among adults)⁷

India

- SCD: 3 million (0.2%) with trait
150,000 (0.01%) with disease⁸
- β -Thalassemia: 45 million (3.3%) with trait
10,000 / year born symptomatic⁸
- HIV: 2.1 million (0.2% among adults)⁹



GGTI includes a Center of Excellence with the capability for cell and gene therapy procedures in Uganda

International Site #1: Joint Clinical Research Center, Kampala, Uganda

A successful indigenous African Institution, a leading Ugandan HIV/AIDS organization, and an international center of excellence

- Network of 6 Centers of Excellence and over a dozen satellite clinics in Uganda, with other clinical centers across sub-Saharan Africa
- State of the art laboratories certified by the WHO, US NIH, and College of American Pathologists
- Latest generation apheresis facility critical for ex-vivo gene therapy
- Commonly perform Red Blood Cell exchange (RBCX) in management of patients with SCD





Take home: Partnerships, Innovation, New Platforms Will Drive Down Cost and Bring Curative Therapies to All Who Need Them



Central
Manufacturing

Point-of-care
Manufacturing



CaringCross



Ben Towne Center for
Childhood Cancer Research

