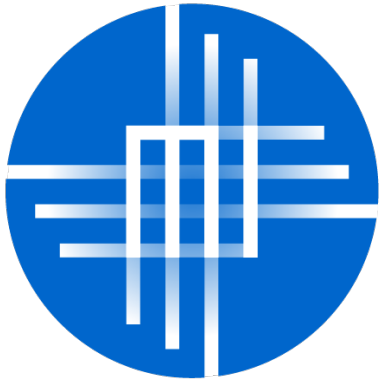


MILKEN INSTITUTE
FasterCures

Stories from the Front Lines of Advancing Therapeutic Development for Patients:

The Research Acceleration and Innovation Network Enters a New Decade

A FasterCures TRAIN Webinar

March 9, 2020

Esther Krofah
Executive Director
FasterCures

Kristin Schneeman
Director
FasterCures

Jill Jarecki
Chief Scientific Officer
Cure SMA

Annette Bakker
President
Children's Tumor Foundation

Albert Roy
Executive Director
Lupus Therapeutics, LLC

TRAIN: The Research Acceleration & Innovation Network

TRAIN's objectives are:

1. To encourage more entrepreneurial philanthropy in medical research
2. To build more and better networks with other R&D stakeholders
3. To enhance the influence of the network

MILKEN INSTITUTE

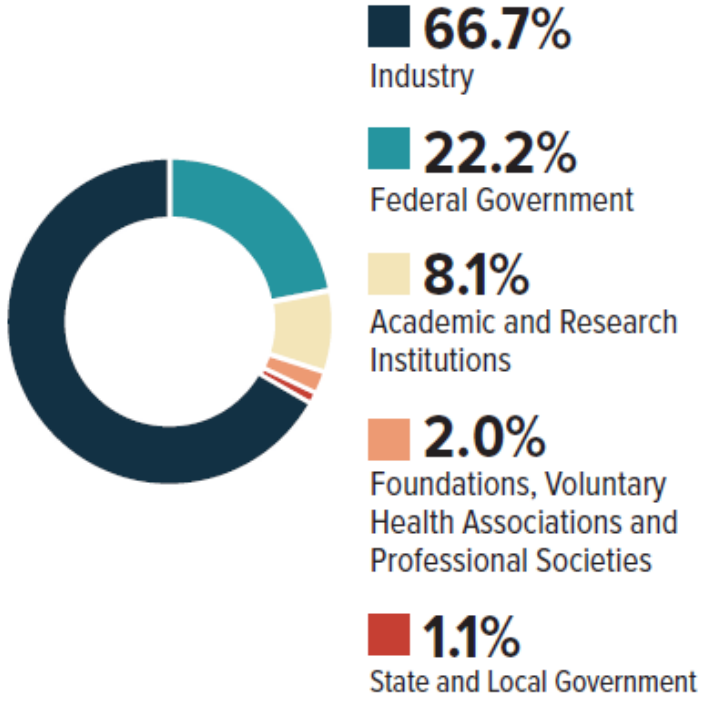
U.S. Health Spending and Medical R&D Investment

Figure 4: R&D Investment as a Percentage of Overall U.S. Health Spending, 2018

Total 2018 Health Spending:

$3.8 trillion

Figure 5: U.S. Medical and Health R&D Expenditures by Funding Source, 2018



Source: Research!America. "U.S. Investments in Medical and Health Research and Development." 2019.

MILKEN INSTITUTE

Philanthropic Investment in Medical R&D in the UK

In 2018, 146 members of the Association of Medical Research Charities invested over £1.3 billion (US $1.677 Billion) in medical research across the UK.

This was 41% of all publicly funded medical research nationally -- more than the Medical Research Council or the National Institute of Health Research!

Source: Member Directory." Association of Medical Research Charities. Accessed March 5, 2020.

MILKEN INSTITUTE

Biomedical R&D Landscape

Only 1 in 10,000 academic discoveries make their way into a new therapy or diagnostics that helps patients

On average, it takes 15 years and US $1 billion to bring a new product to the market

773 FDA-approved orphan drugs as of 2019

<3% all of US funding for R&D from philanthropic sources

MILKEN INSTITUTE

Source: Stevens, Melissa L. “Medical Philanthropy Pays Dividends.” 2019.

Private Investment Increasing, But Challenges Remain

Positive Trends

- In 2017, the life science venture capital industry saw record financings, and funding is up over 250% since 2013
- 2018 saw approximately 700 deals in pharma and biotech in R&D investment (US $17 B)

Continuing Problems

- NIH funding is higher than ever, but it is still operating at a loss after inflation and its purchasing power has decreased by 22%
- This threatens the pipeline of scientific talent, delays scientific independence and stunts research
- "Valley of death"- the gap between discovery and the point at which a company is willing to step in – still exists, and more funding is needed to support preclinical and clinical work to determine scientific proof of concept

MILKEN INSTITUTE

Source: Stevens, Melissa L. "Medical Philanthropy Pays Dividends." 2019.

Impatient Patients Drive Progress

Matthew Herper, Forbes Staff
I cover science and medicine, and believe this is biology's century.

PHARMA & HEALTHCARE | 2/05/2013 @ 10:51AM | 653 views

Forbes Health Summit: How Patient Groups Are Changing Biotech

This is one of a series of posts that presents, nearly in its entirety, the first annual Forbes Healthcare Summit that was held on December 5, 2012, in Allen Room at Jazz at Lincoln Center in Manhattan. Two hundred and th two executives, entrepreneurs, thinkers and policy makers gathered to ta trade ideas, and grapple with a big-picture conversation about the health system. Video of almost every single panel is included.

Panel: **Philanthropy in Healthcare – When Patients Become Catalysts for Change**

FierceBiotech
THE BIOTECH INDUSTRY'S DAILY MONITOR

FIERCEBIOTECH SPECIAL REPORT

FOUNDATIONS FUEL RISKY BIOTECH VENTURES

BY ARLENE WEINTRAUB

The Boston Globe
WEDNESDAY, JUNE 20, 2012

In the news

Patients drive new drug research
Pharmaceutical industry, FDA respond to personalized demands

Forbes
PATIENT POWER
The 100 Most Powerful Women

The New Power Players in Drug R&D Are Wearing Bright T-Shirts

Luke Timmerman | 10/29/12 | Follow @ldtimmerman

Xconomy

See all those people signing up for the 10K charity run/walk in your hometown this weekend? Those folks in your Facebook photo album, decked out with colorful T-shirts and uplifting messages about fighting some disease?

You could easily have written off many of these nonprofit fundraisers a few years ago as well-intended, but ultimately ineffective, efforts for coming up with cures. The real action, you could have argued, was only happening in the investor-

BioBeat

SHARE AND COMMENT

Leave a Comment

Reprint

Story

34 Like

3 +1

Bloomberg Markets

…Frustrated with the sluggishness, or nonexistence, of medical research…a small band of wealthy parents whose children have serious illnesses are spending millions of dollars to fund drug development...The principles they apply in their jobs -- **managing complicated tasks, making investments and expecting positive results -- translate to their new endeavors.**

"…patient groups with an entrepreneurial bent have become the drug industry's new power brokers."
- Forbes

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What is Venture Philanthropy?

"Takes concepts and techniques from venture capital finance and high technology business management and applies them to achieving philanthropic goals."

"Treats funding as an investment rather than as the traditional concept of a charitable grant, with corresponding expectations of return on investment, operating efficiencies, and management oversight."

"Philanthropy with an opinion."

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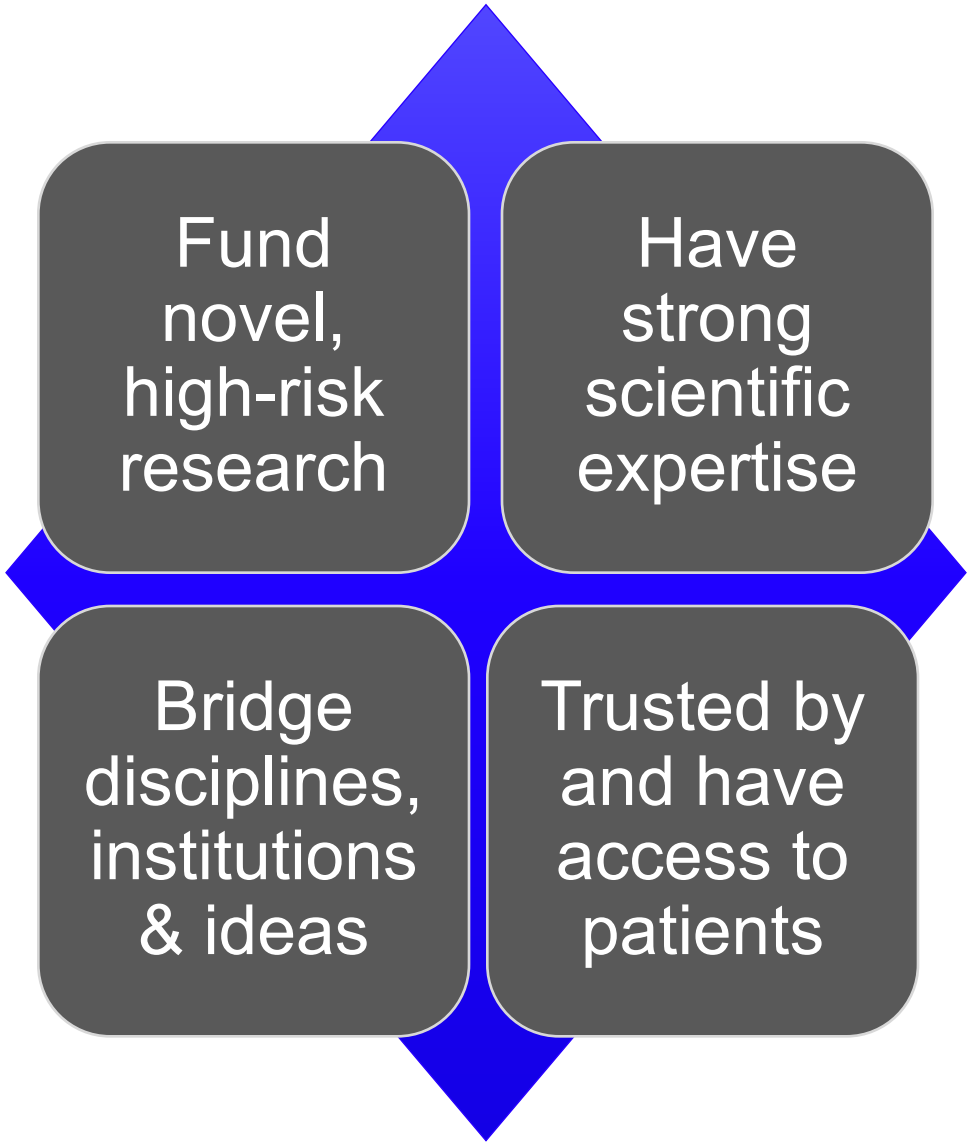
Characteristics of Venture Philanthropies



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Jill Jarecki

Chief Scientific Officer

Cure SMA

Faster Cures Webinar

March 9, 2020

Jill Jarecki, PhD
CSO

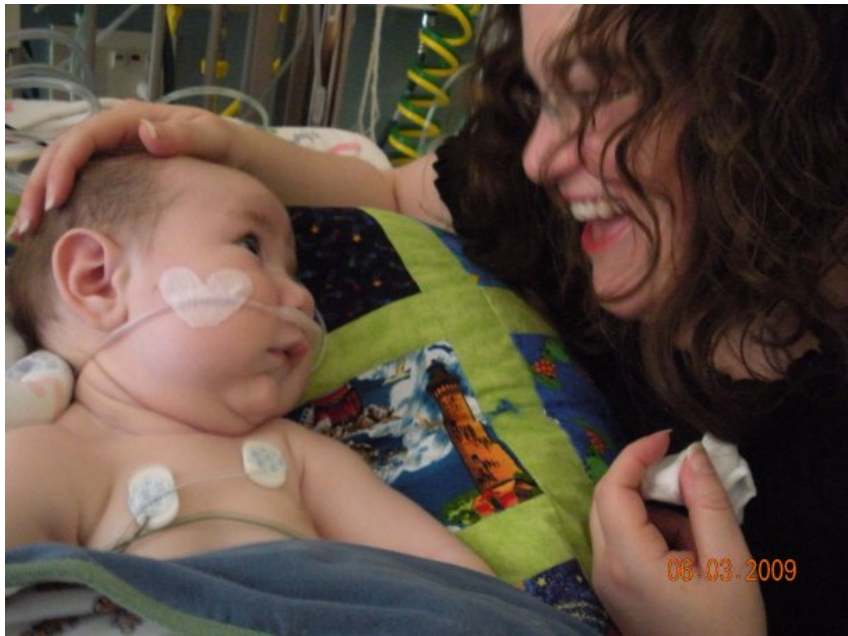
cure SMA

Make today a breakthrough.

Cure SMA

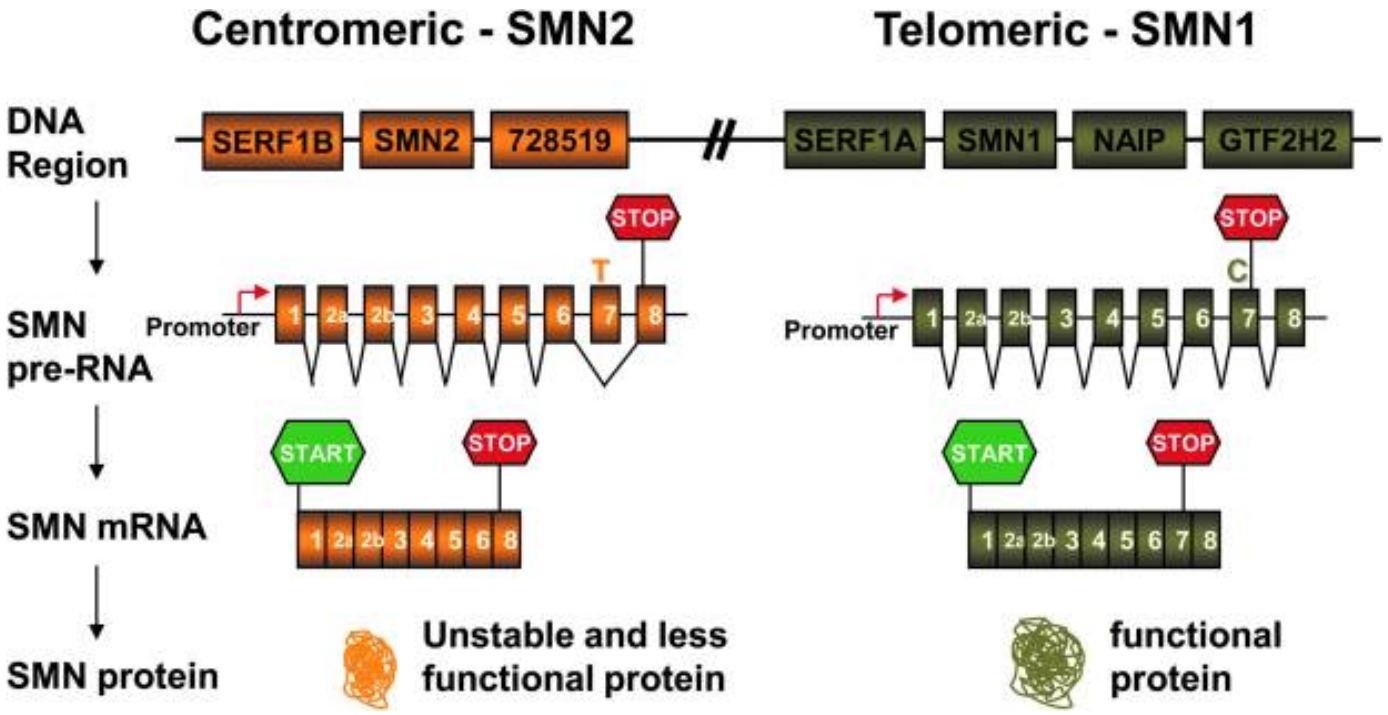
We fund groundbreaking research and provide families the support they need for today.

- Annual budget of $15M
- $80 Million in research funding
- 36 Chapters in the US
- 8,000 affected individuals in membership database
- 500 newly diagnosed contacts annually
  - Newly diagnosed care and info packets
  - Info on clinical trial recruitment
- 4,000 families obtain services annually



SMA Background

- Autosomal recessive disease of motor neurons
- Most common form genetic infant mortality, with 1 in 11,000 live births
- 95% of cases caused by SMN1 gene homozygous deletion
- SMN2 disease modifier but cannot compensate for loss of SMN1



FDA approved drugs:

-Spinraza – Approved December 2016

-Zolgensma – Approved May 2019

-Risdiplam – PDUFA data May 2020

Important Research Investments to De-Risk Clinical Development and Attract Investment

- **Basic and Drug Research**
  - Disease pathophysiology (when, where, what, how)
  - Creating research tools (screens, animal and cellular models)
  - Discovering / validating therapeutic targets (seed ideas for drugs)
  - Directed IND enabling studies with best therapeutic avenues
- **Enabling Clinical Development**
  - Collecting natural history (understanding your patient population)
  - Developing outcome measures and understanding sub-group sensitivity
  - Discovering biomarkers for POC for early clinical trials
  - Defining clinical meaningfulness for your patients
  - Organizing and educating your patient population for trials
  - Developing a relationship with FDA

Cure SMA Research Funding Strategy

Discovering therapeutic approaches with basic research

- 127 PI-driven basic research grants for $15M since 2004
- Ensuring funded science is well controlled and reproducible
- Establishing fair and transparent funding process with SAB
- Greater emphasis early on: 100% before 2000 but 30% of budget today

De-risking early stage drug programs to leverage investment

- $21M for 14 programs by TAC (screeners, chemists, toxicologists, pharmacologists)
- IND enabling studies (med chem, GLP tox, pharmacology)
  - Well-defined, goal-oriented projects with good prospects for IND
  - Joint steering committee develops and decides on milestones
  - Cure SMA secures return on investment
- Provide subject matter expertise for companies new to SMA
- Provide practical drug discovery advice for academics
- Principle: investment until IND; transition to industry / government

Shifting Research Goals with Success: Combination Therapies and Multiple Drug Options

- **Novel target ID and combinations for maximally effective treatments for all SMA types and stages**
  - Identify non-SMN drug targets
  - Test combinations with SMN up-regulating drugs
  - Optimized SMN enhancing therapies: next in class drugs
- **RFPs in basic & drug research geared to these goals since 2016**

Encouraging Collaboration

- **Annual SMA Conference**
  - Family Meeting - 2000 patients and families
  - Researcher and Clinical Care Meeting – 700 attendees
  - Many industry advisory boards and focus groups
  - Clinical trial trainings
- **Working groups from Academia & Medicine**
  - RUSP Submission Working Group
  - Treatment Algorithm Working Group
- **Aligning Industry Partners for Community Benefit**
  - NBS Coalition
  - SMA Industry Collaboration

Industry Collaboration: 7 companies co-funding and shaping projects with $2.1M budget

Regulatory Interactions

- Patient Focused Drug Development Meeting with FDA in April 2017
- Risk / Benefit Survey for SMA - published 2019
- Economic Burden of Disease Study - manuscript in preparation

Increasing clinical trial site capacity

- Identifying and training up to 20 new trial sites
- PT and CC toolkits and in person workshops (https://www.curesma.org/clinical-trial-readiness-toolkits/)

Education of HCPs & patients to reduce diagnosis time

- Educational campaign with professional societies (AAP, AAN, CNS, NORD, CNF)
- Concerned Parent and HCP website called **SMArt MOVES**
- Physician Surveys

Patient Reported Data Project

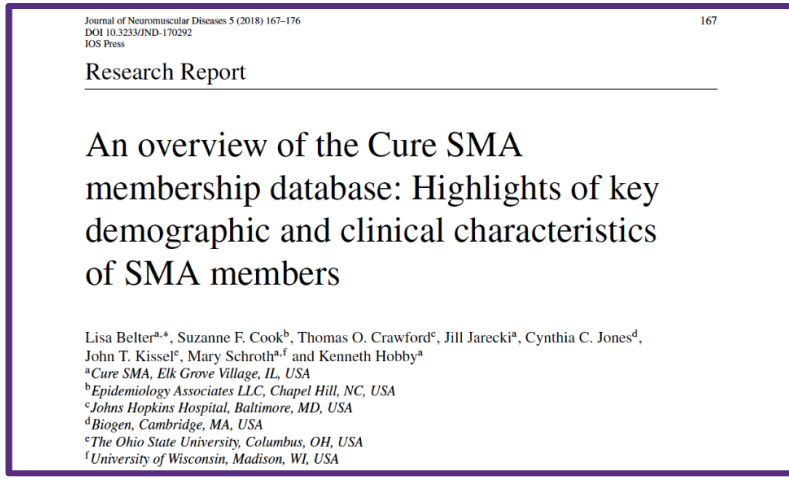
- Annual community survey and new contacts reports

Registry Group

- GUID development

Organizing, Tracking, & Educating Patient Community

- **8,300 affected individuals in database**
- **4,089 contacts: July 2009 - January 2020**
  - Over 500 newly diagnosed annually
  - Type, incidence/prevalence, disease burden, geography, diagnostic journey, survival
- **Supports Community**
  - Education, Care packages, informational packets, and scholarships for conference
- **Research recruitment efforts**
  - 15 requests per year
- **Clinical trial recruitment efforts**
  - 1100 patients into 15 clinical trials
- **Real time changes: annual survey**
  - Shared with industry, payers, & regulators

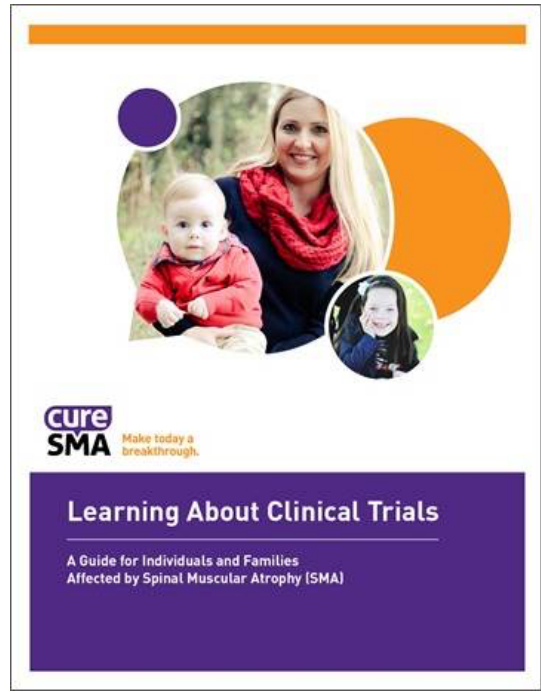


Journal of Neuromuscular Diseases 5 (2018) 167–176
DOI 10.3233/JND-170292
IOS Press

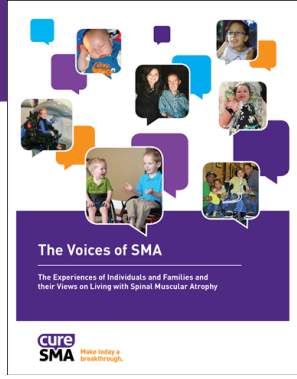
Research Report

An overview of the Cure SMA membership database: Highlights of key demographic and clinical characteristics of SMA members

Lisa Belter[a,*], Suzanne F. Cook[b], Thomas O. Crawford[c], Jill Jarecki[a], Cynthia C. Jones[d], John T. Kissel[e], Mary Schroth[a,f] and Kenneth Hobby[a]
[a]*Cure SMA, Elk Grove Village, IL, USA*
[b]*Epidemiology Associates LLC, Chapel Hill, NC, USA*
[c]*Johns Hopkins Hospital, Baltimore, MD, USA*
[d]*Biogen, Cambridge, MA, USA*
[e]*The Ohio State University, Columbus, OH, USA*
[f]*University of Wisconsin, Madison, WI, USA*



FDA Regulatory Interactions and Patient-Focused Drug Development



2020 — Critical Path Innovation Meeting, *May 2020*

2017/19 — Patient Focused Drug Development Meeting (Drs. Dunn & Marks attended), *April 2017*
VoP report on FDA website; Benefit / Risk survey (published Clinical Therapeutics, 2019).

2016 — Listening session with FDA Commissioner, Dr. Califf, *December 2016*

2015 — Voices of SMA Booklet, *September 2015*
Shared with FDA leadership, including Dr. Woodcock.

2015 — In person patient meeting and calls with FDA on White Oak Campus

2013/14 — Patient focus groups on meaningful benefit and impact on daily living
Two papers published in BMC and sent to FDA staff.

2011/14 — Scientific Meetings: NINDS -So SMART Outcomes Meeting, *June 2014*
Biomarker Meeting, *2011*

Ongoing — FDA Attendance at SMA Annual Conference,
i.e., Dr. Moscicki of CDER in 2014.

Ongoing — Providing formal commentary on FDA guidance on multiple occasions

Current Projects and Next Steps

- **Newborn screening in all 50 states – 70% of births end of 2020**
  - 19 states fully implemented, 14 adopted not implemented, and 5 pilots
- **Approved drugs with maximal efficacy for all SMA stages & types**
  - SMN up-regulating drugs with different routes of administration
  - Combination therapies with novel targets
- **Clinical Center Network (CCN)**
  - Develop and disseminate evidence based SMA standard of care
  - More sites to deliver specialized SMA therapies & care
  - 50/50 adult and pediatric prevalence disease
- **Data Collection through Clinical Data Registry (CDR)**
  - 18 current sites with 50 by 2022
  - Improve care and document efficacy post market
- **Direct local services in addition to national delivery**

cure SMA

Summary

- Develop strategic research plan to de-risk disease drug development to enable pharma investment
- Shift plan / research strategy at different stages
- Collaborations and resources in addition to $ are critical to success drug development
- Organize and educate patient community to enable clinical trials, data collection, & positive community environment
- Give patient community a voice by educating FDA, insurers, and drug developments with both data and stories
- Plan for future success: think early for NBS, drug access, & post-marketing data collection

Annette Bakker

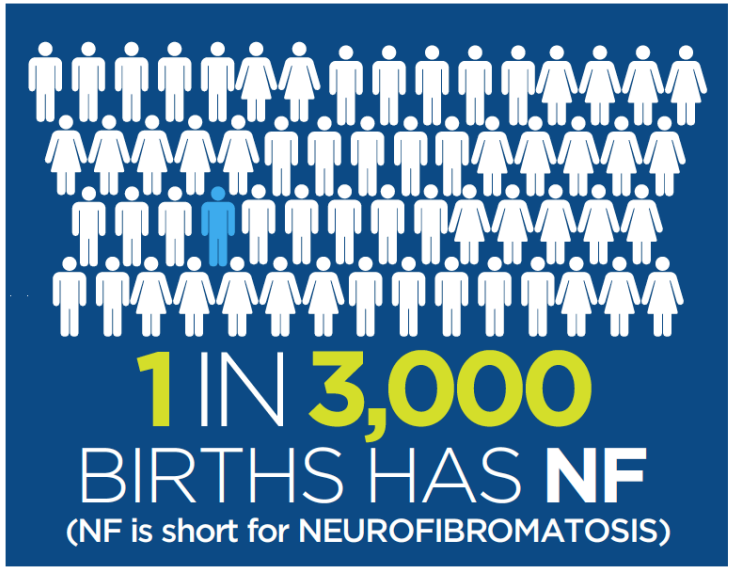
President

Children’s Tumor Foundation

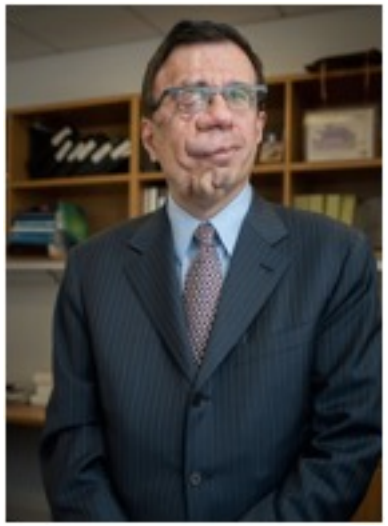
Children's Tumor Foundation
ENDING NF
(Neurofibromatosis)

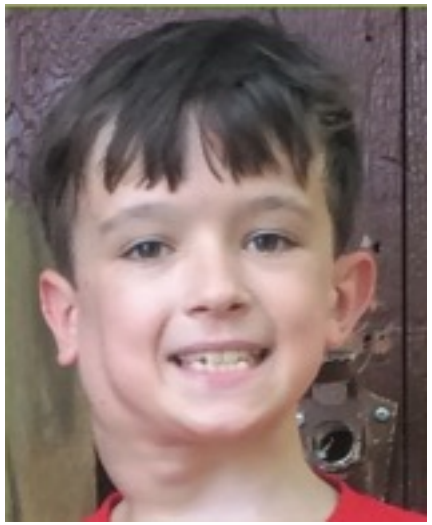
Annette Bakker
abakker@ctf.org

What is neurofibromatosis (NF)?



Living with NF



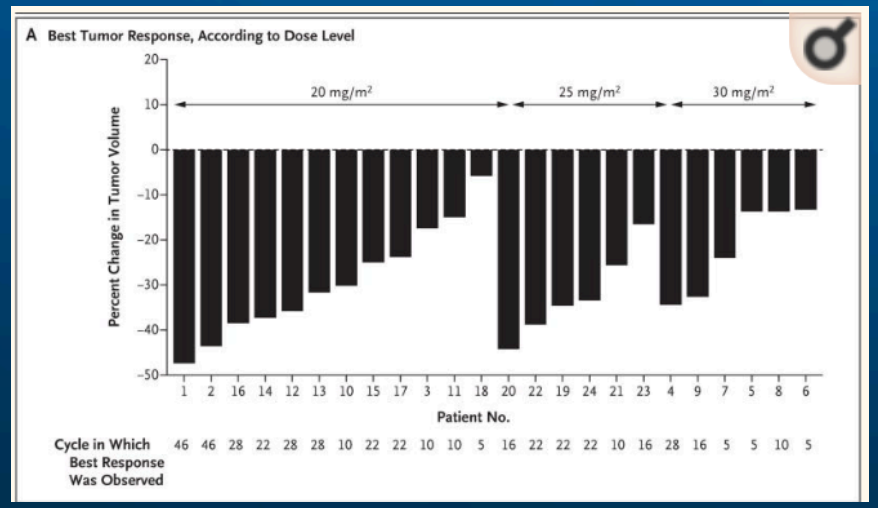


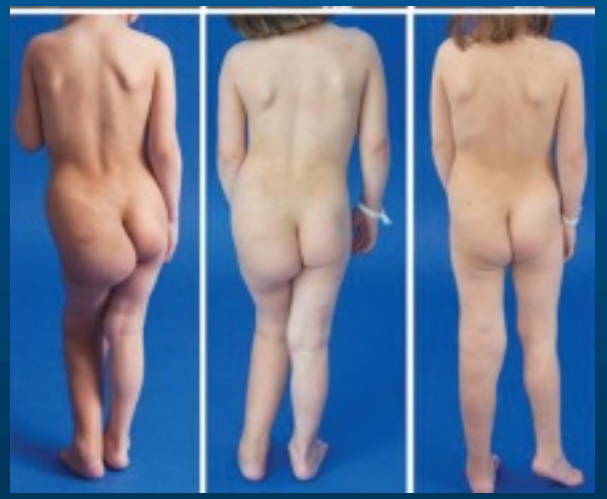
Top 5 wins / Last 5 years

- Created diversified R&D portfolio – first ever in NF
  (drugs, biologics, gene therapy)
- Built vibrant patient, research, funder, and data community
- Attracted pharma/biotech into NF
- Tripled the number of clinical trials for NF
- And…

CTF helped bring Selumetinib to FDA

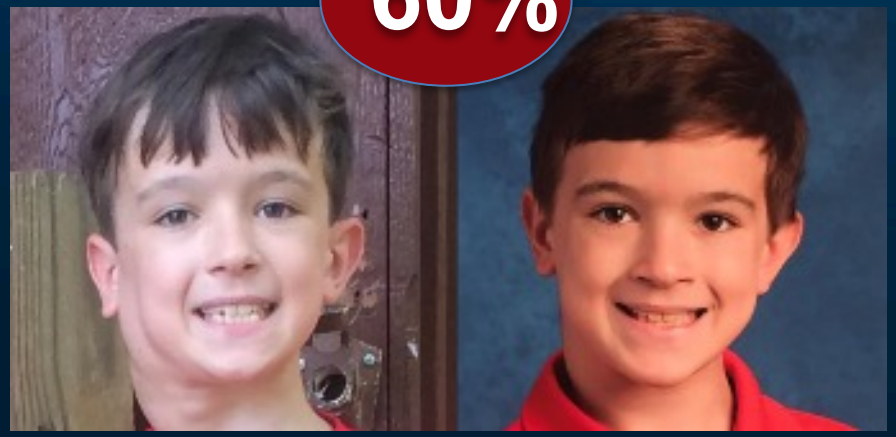
CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

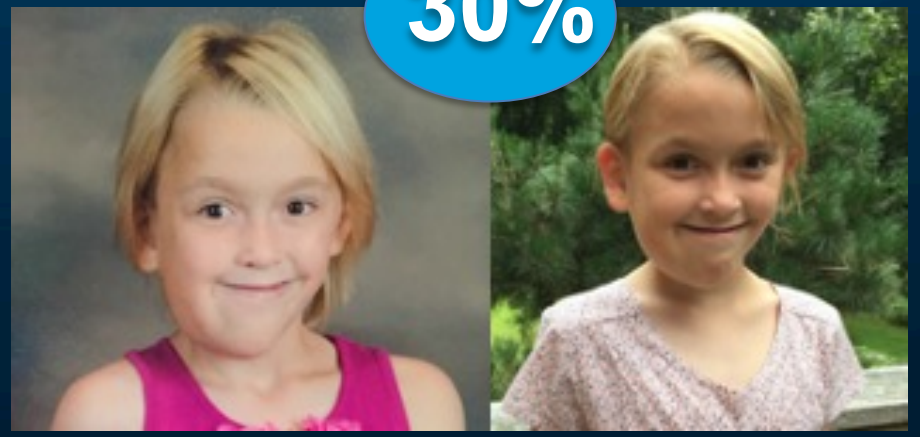




NEJM 2016, 375 :2550

At FDA Now!



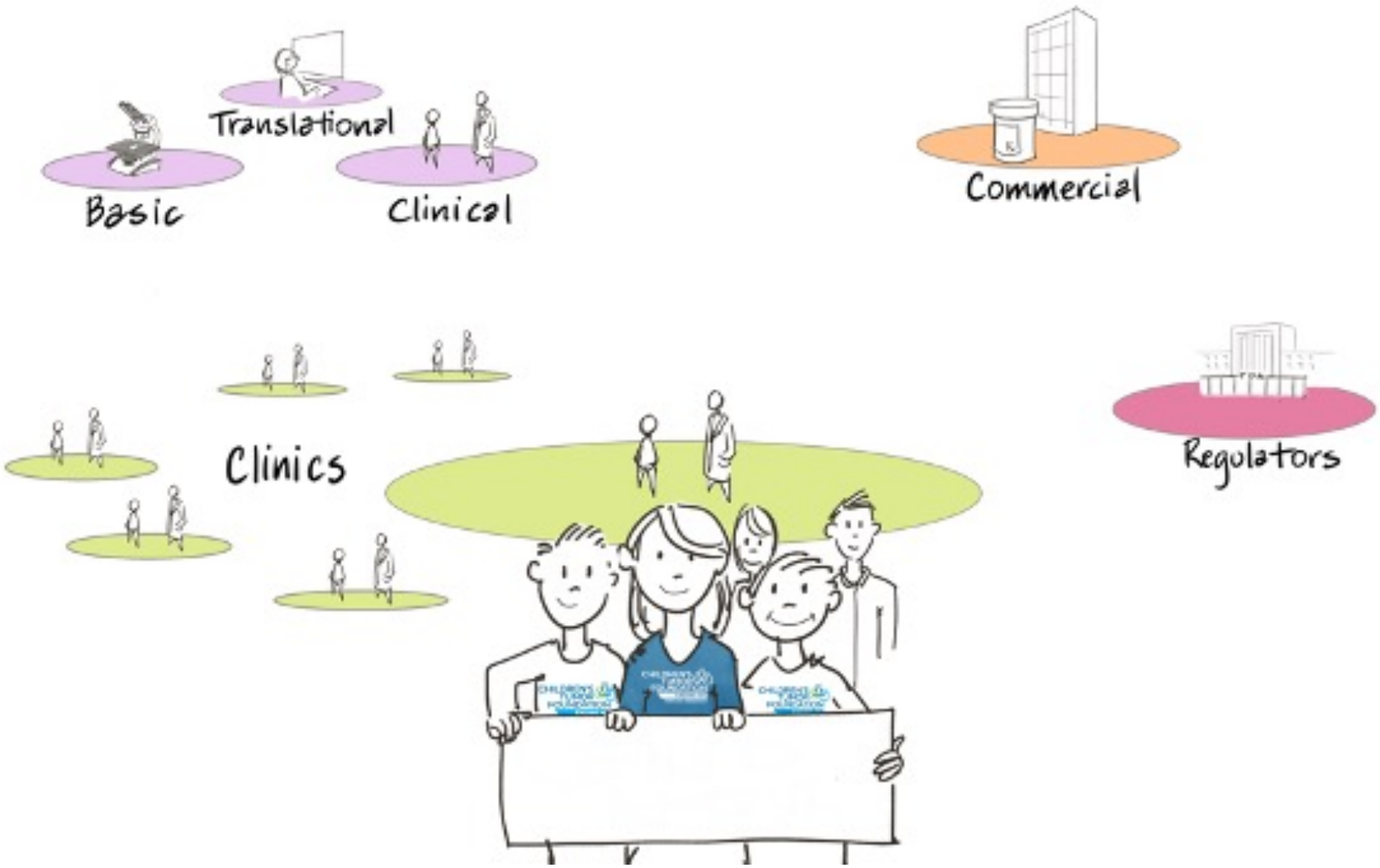


How did we do it?

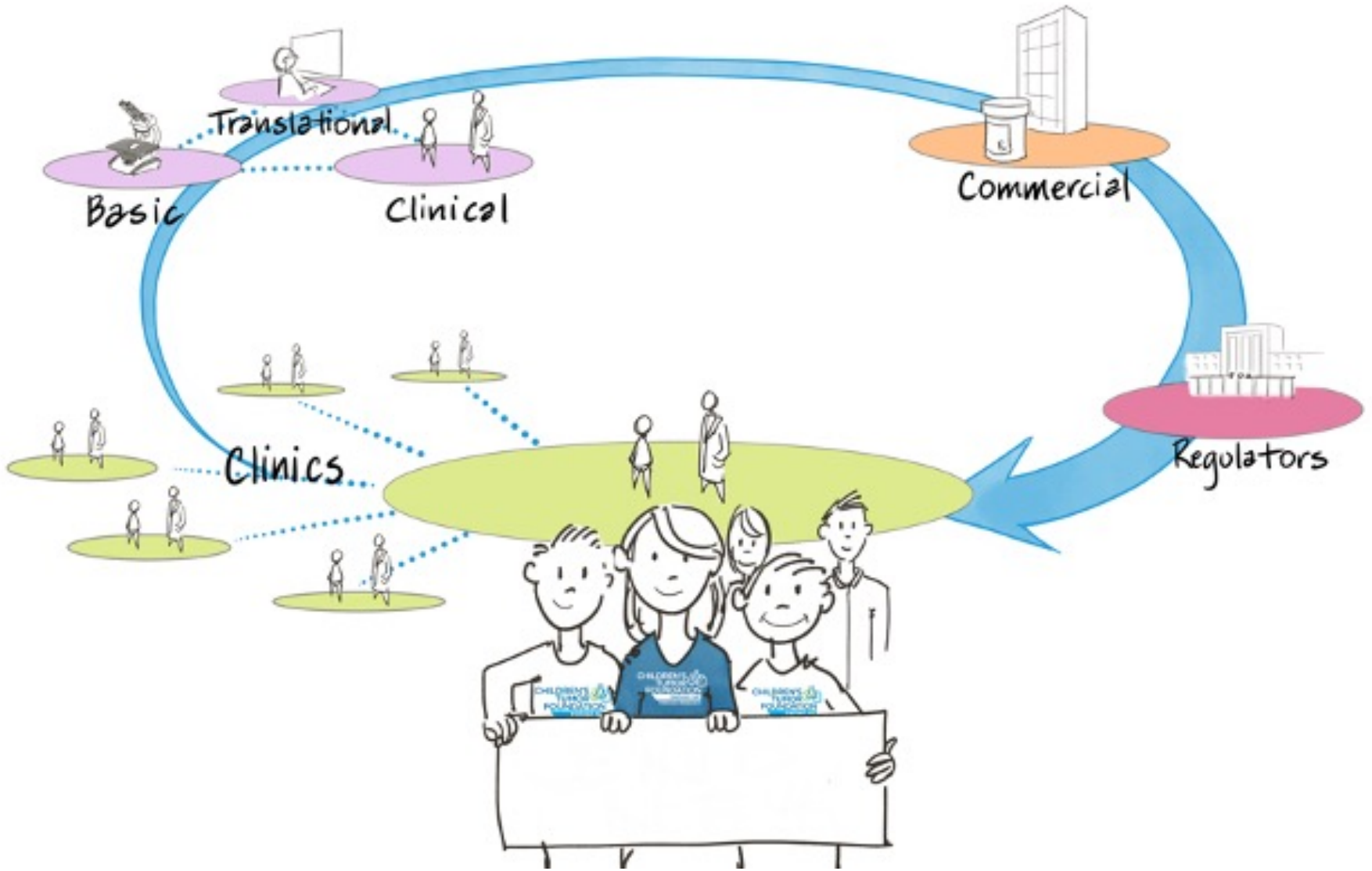
Children's Tumor Foundation is:

- The global **connector**
- The research **disruptor**
- The pharma **attractor**

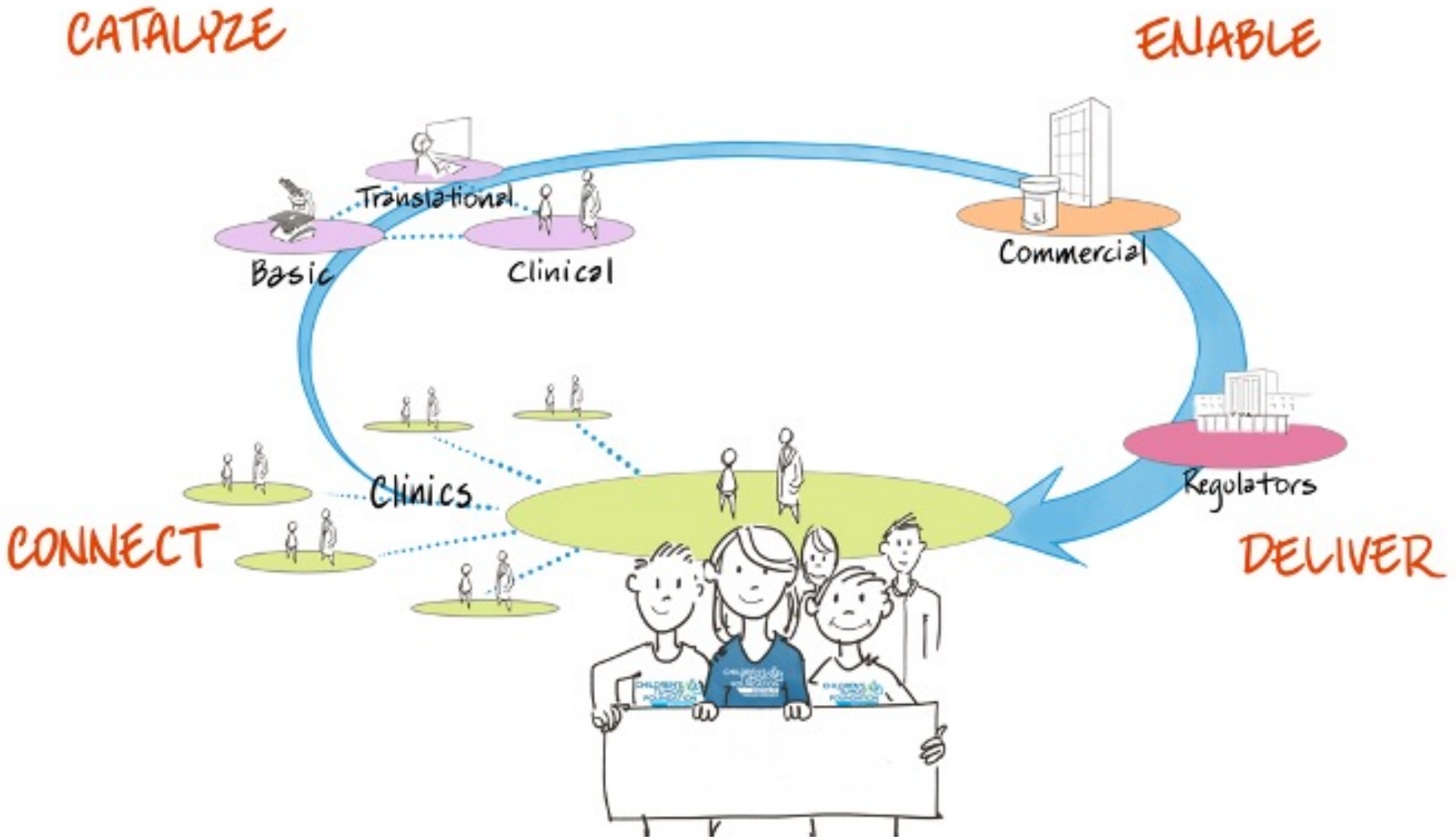
Traditional siloed R&D ecosystem



CTF ambition: unite to End NF

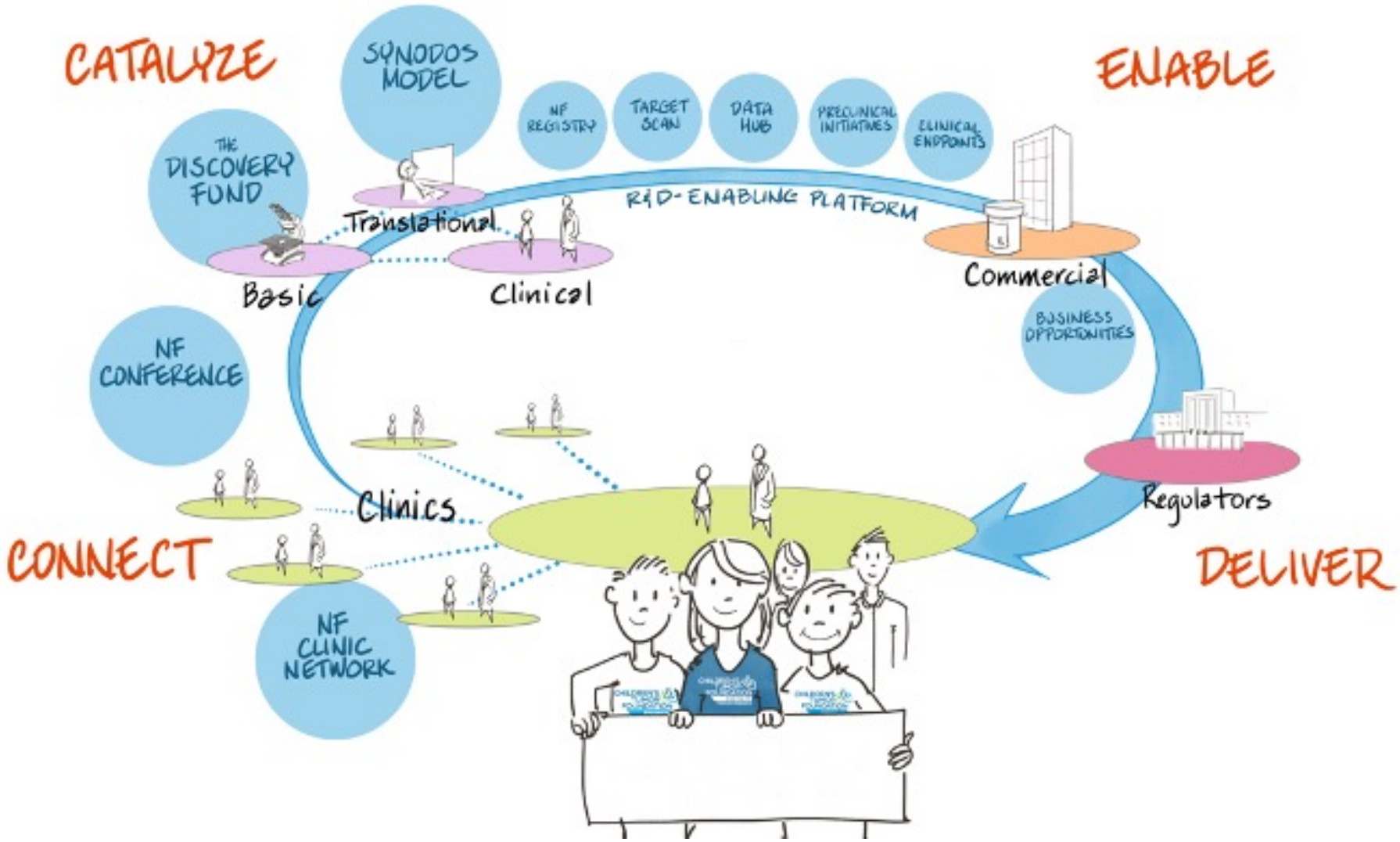


Connect · Catalyze · Enable · Deliver



Children's Tumor Foundation Initiatives

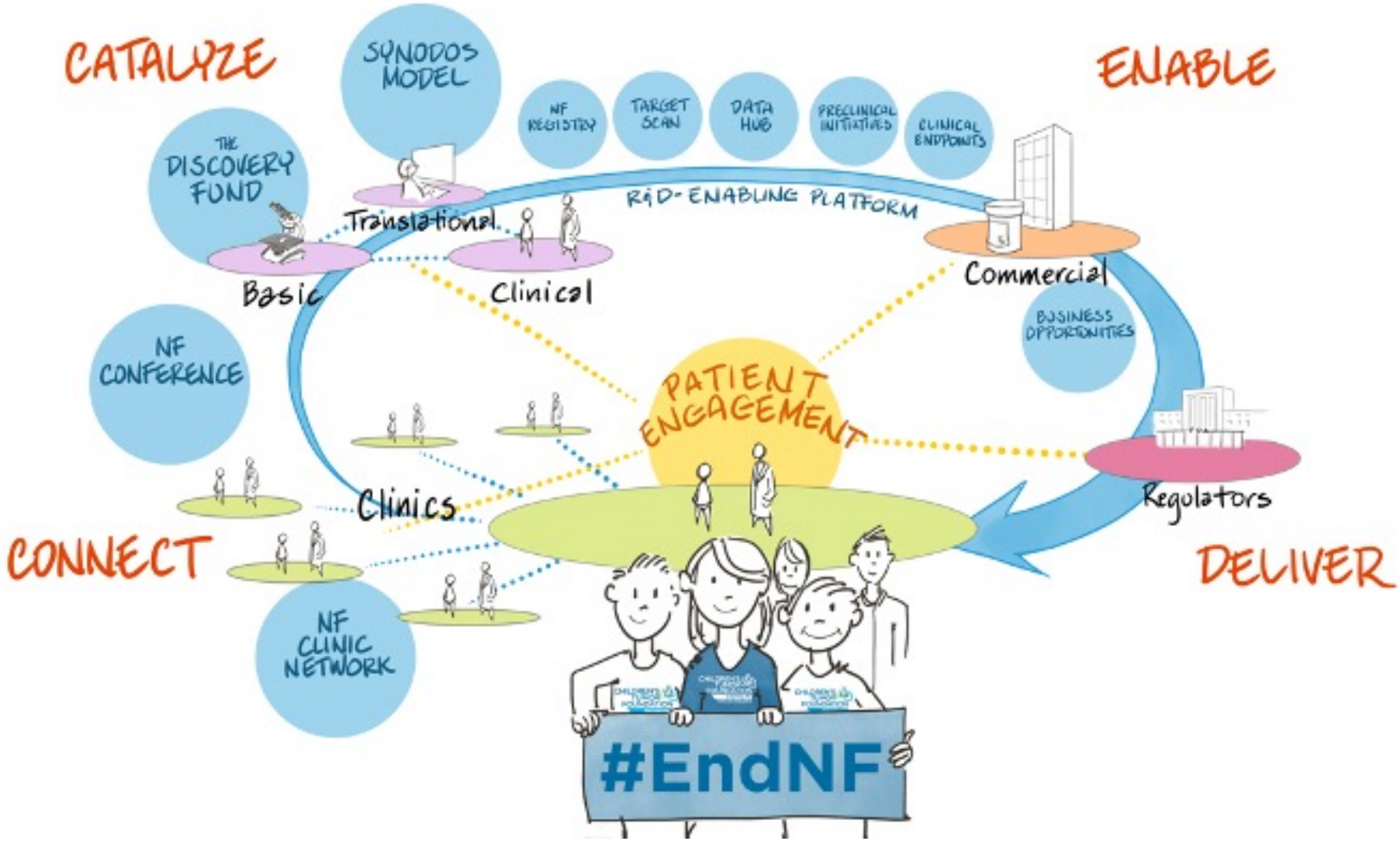
CHILDREN'S TUMOR FOUNDATION
ENDING NF
THROUGH RESEARCH



R&D Enabling Platform – by the numbers

CTF - NF Platform	
NF Clinic Network	15,000 patients/ 56 clinics
NF Patient Registry	Almost 10,000 patients, 98 countries
Open Biobank – in partnership with Indiana University	Hundreds of tissues for all forms of NF
NF Data Portal www.nfdataportal.org	Thousands of data sets Co-funded with other NF funders
Key Opinion Leader networks	Access to key researchers/clinicians
Preclinical Models	Cell lines at ATCC NF Preclinical initiative (under reconstruction)
Path to Approval	Consensus criteria developed and published

Patients as partners – united to End NF



Thank You

CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

Join us in the fight to End NF

ctf.org

Albert Roy

Executive Director

Lupus Therapeutics, LLC

FasterCures: Stories From the Front Lines of Advancing Therapeutic Development for Patients

Albert T. Roy
Executive Director
Lupus Therapeutics, LLC
March 9, 2020

Lupus THERAPEUTICS
an affiliate of
LUPUS RESEARCH ALLIANCE

Lupus Therapeutics Company Profile

Formation

- Affiliate of Lupus Research Alliance
  - Formed in January 2018
  - 501(c)3 status

Governance

- Lupus Therapeutics (**LT**) Board of Directors
  - Legal/Fiduciary responsibility
  - Board Composition: LRA Board & External members (VC, industry, academic)

Function

- Coordinate *Lupus Clinical Investigators Network (*LuCIN) activities
  - Lupus focused clinical trial network
  - >50 Academic research centers in US & Canada
- Financially incentive LuCIN sites to become and remain enrollment ready for LuCIN-sanctioned trials
- Provide study start-up and consultative service offerings to Industry

Lupus THERAPEUTICS
an affiliate of LUPUS RESEARCH ALLIANCE

Lupus…The Unfortunate Truths

- Lupus is a chronic, potentially fatal, autoimmune disease
- Rather than protect against infection, the immune system of lupus patients attacks their own tissues and organs — kidneys, brain, heart, lungs, blood, skin and joints
- Lupus has no known cause

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The Need For Better Treatments

- Only one new drug (Benlysta) has been approved for *treatment* in the last 65 years
- Today's treatments offer lupus patients only temporary relief — and cause significant, dangerous or debilitating side effects
- LRA initiated a new research program to address the slow pace of development of new therapies for lupus
- Originally focused on re-positioning FDA-approved drugs for lupus
  - Secondary goal: Redirect drugs in development toward lupus

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Challenges in Conducting Lupus Clinical Trials

- Heterogeneous patient population
- Lupus studies carried out globally often do not follow best practices in lupus diagnosis and study recruitment
- Difficult to recruit African American patients – lack patient trust
- Patient uneasiness related to modifying treatment – fear of ”rocking the boat”
- Lupus clinical investigator community – culture of research, not prevalent

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Our Vision

- Overarching Goal – Identify, de-risk, and accelerate the conduct of novel lupus clinical trials through a research consortium model, LuCIN

- Core Constituents:
  - Pharma/Industry – Drug developers/trial sponsors/source of revenue
  - KoLs/Investigators – point of care/trial conduct
  - Patients – who we serve

- Points of Differentiation:
  - Broad Lupus footprint/research reputation
  - Exclusively Academic-led Trials Network

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Achieving Goal

- Identify –
  - LuCIN/KoL referrals
  - Pharma interactions (reactive/proactive approaches)
  - Data/Literature Mining

- De-risk –
  - Clinical trial infrastructure - LuCIN
  - Proper drug candidate vetting/prioritization (SABs)
  - Novel study design review/approaches (LuCIN PRC)
  - Active patient engagement (Ad boards)

- Accelerate - Site Management Organization Services
  - Site identification/investigator recruitment
  - Study Start-up services

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Our Approach

To a Turn-key Network

Establish LuCIN

Academic sites

- >50 sites in US and Canada
- >150 investigators
- >23,000 patients in clinic population
- Incentivized (funded) to support enrollment

Physician Leadership

- Governance Structure, Working Committees

Industry-led & Investigator-led Clinical Research

Suite of Service Offerings

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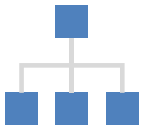
Lupus Therapeutics Suite of Services

A Options | **B** Options | **C** Options | **D** Options



Advisory Board

- Review drug candidate(s) and clinical development programs of industry

Protocol Design & Development

- Review protocol design, endpoint development, PRO development and selection

Study Start-up

- Conduct feasibility, contract, budget negotiation
- Facilitate PI/site engagement
- Assess site operational and logistical challenges
- Identify unique site or patient specific burdens

Patient Engagement

- Advisory Panels
- Obtain feedback on
  - protocol, consent,
  - risk/benefit,
  - trial burden
  - packaging
  - trial recruitment materials
- PALS Program

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Our Approach…In Action

- Provided scientific rationale to Janssen to repurpose Ustekinumab (Stelara) in SLE
- Positive Phase II study in SLE - 2018
- Phase III SLE study recently closed to accrual (January 2020)
  - Top-line results – January 2021
- March 2021 – forged additional partnership with Janssen to repurpose second second(confidential) in Lupus Nephritis
  - Planned Phase II study 2Q2020
- Ongoing discussion w/ Lilly for TBN asset

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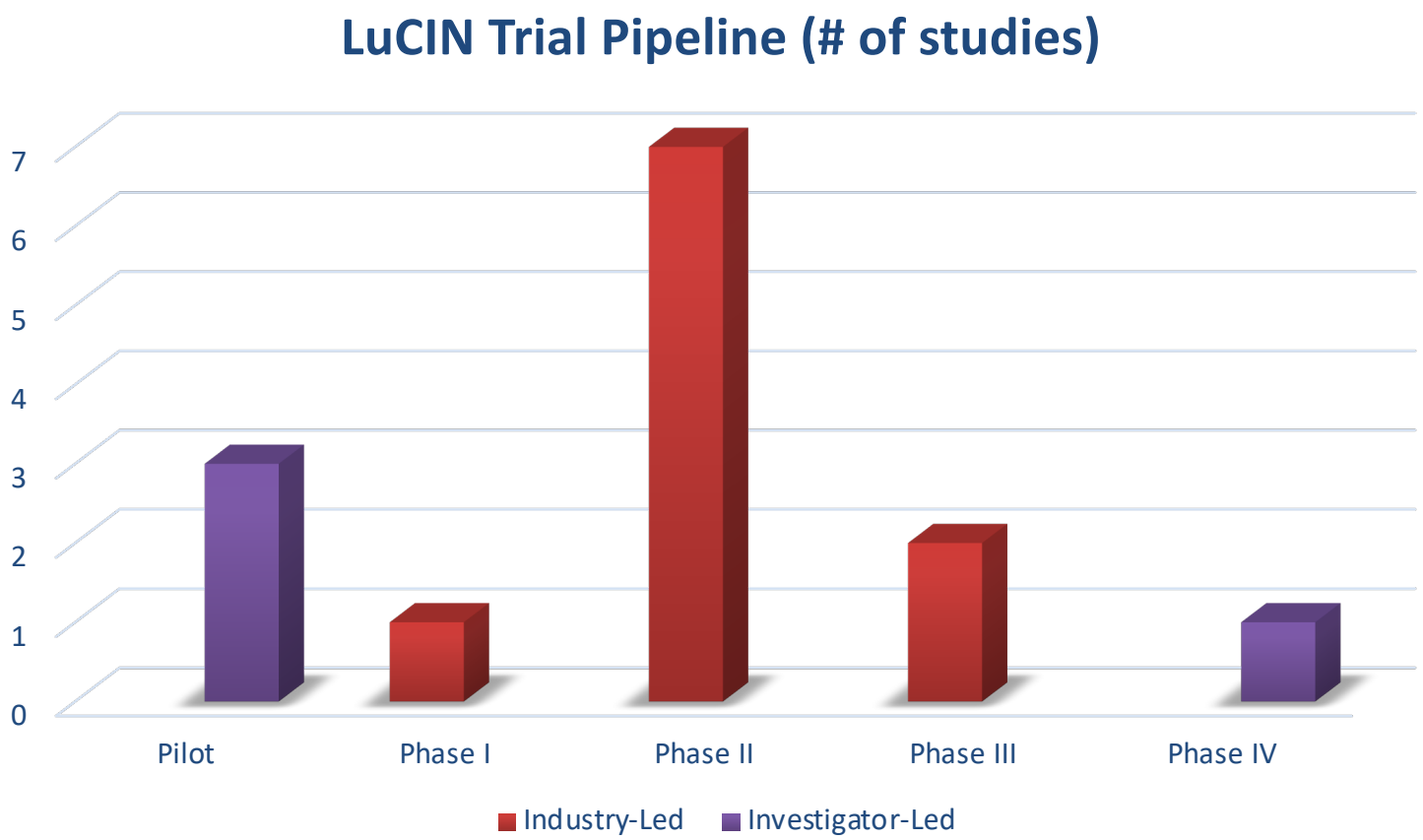
Phase I	Phase II	Phase III	Pilot/IICT
Takeda	Bristol-Myers Squibb		HORIZON PHARMA
	Bristol-Myers Squibb		Pfizer
	janssen	janssen	AkerBioMarine
	AMGEN	ucb	
	Celgene		
	Lilly		
	EMD SERONO		

Achievements



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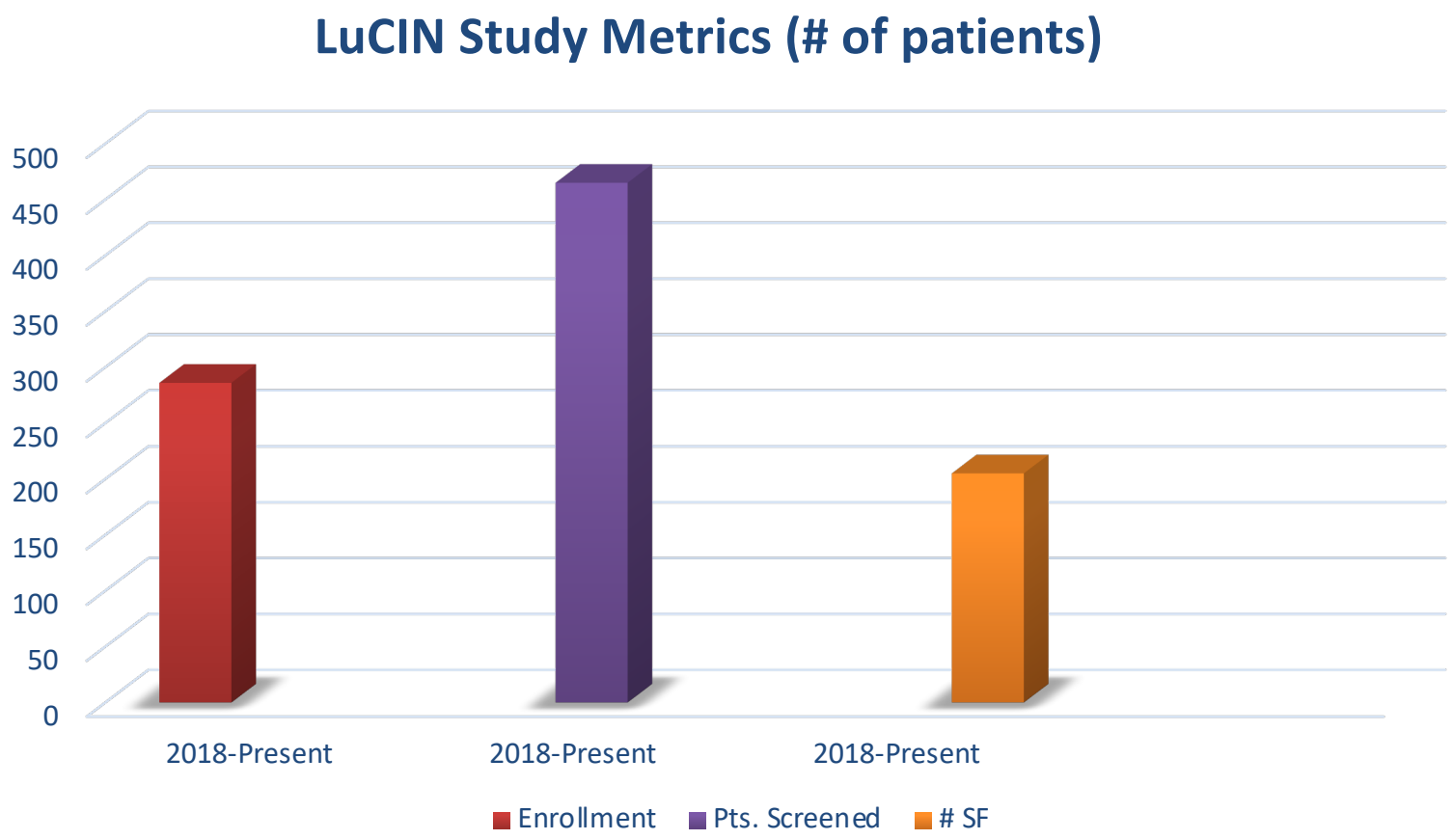
Achievements (cont.)



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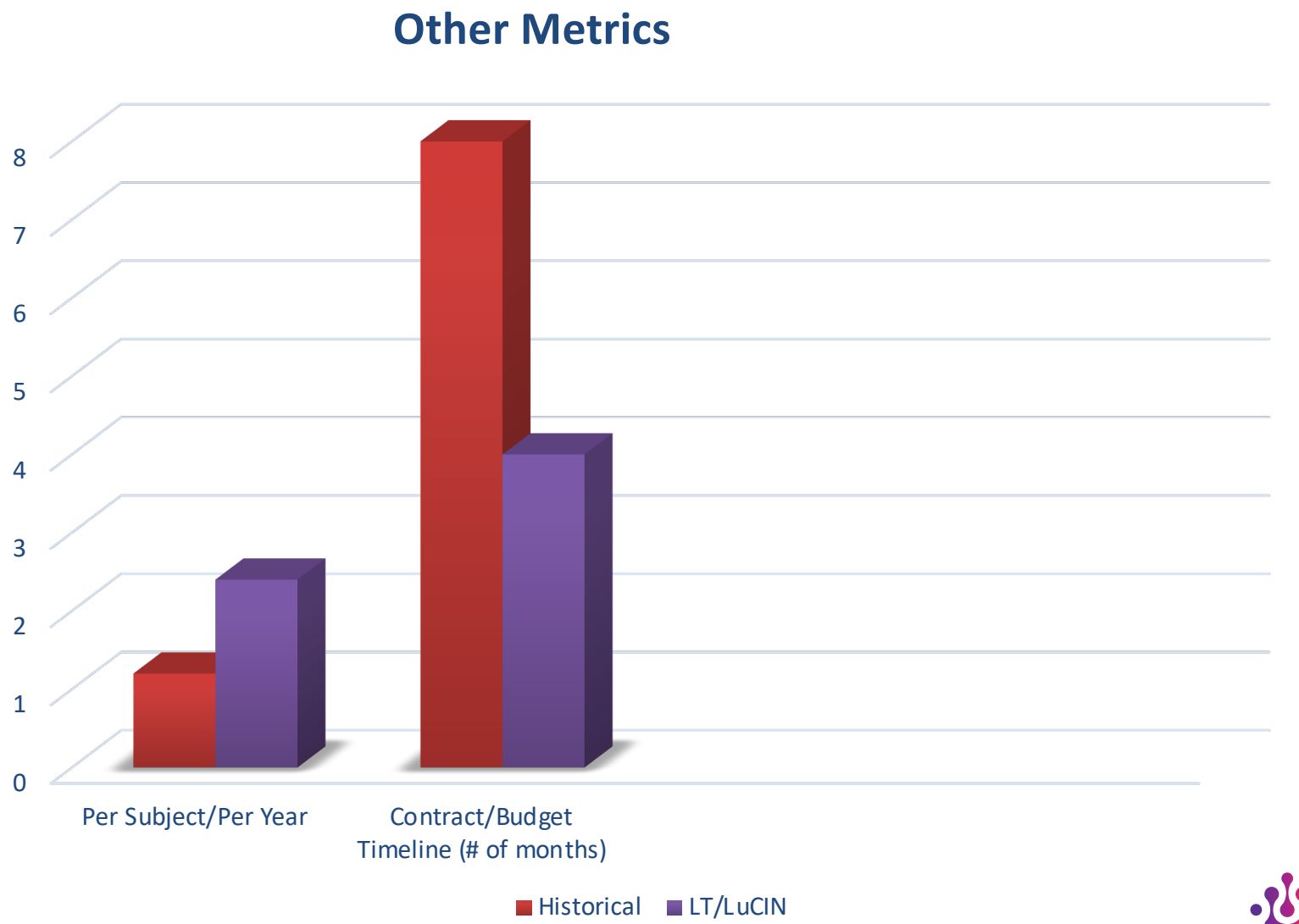
Achievements (cont.)



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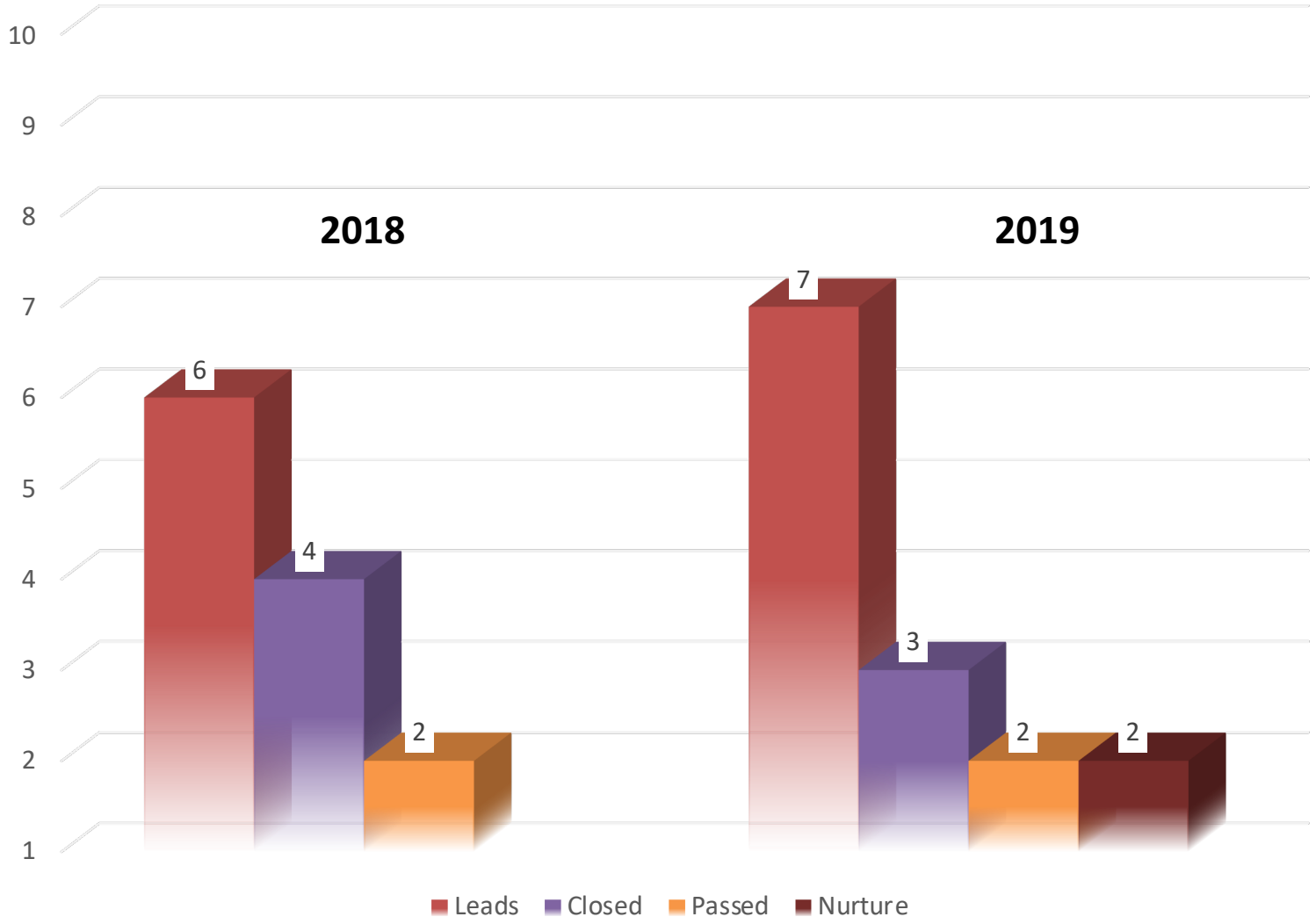
PIPELINE CONVERSION



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Challenges

- Overcoming industry perception that Lupus is a “graveyard” for Drug Development
- Establishing brand equity within the drug development community
- Services compete w/ CROs – fully integrated with industry
- Paradigm shift slow with academic investigators – creating a “culture of research”
- Overcoming patient reluctance to participate in lupus clinical trials

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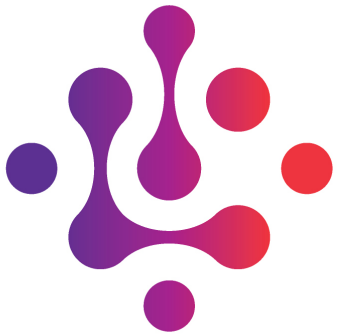

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