# Lessons Learned from Acceleration in Pediatric Oncology Programs

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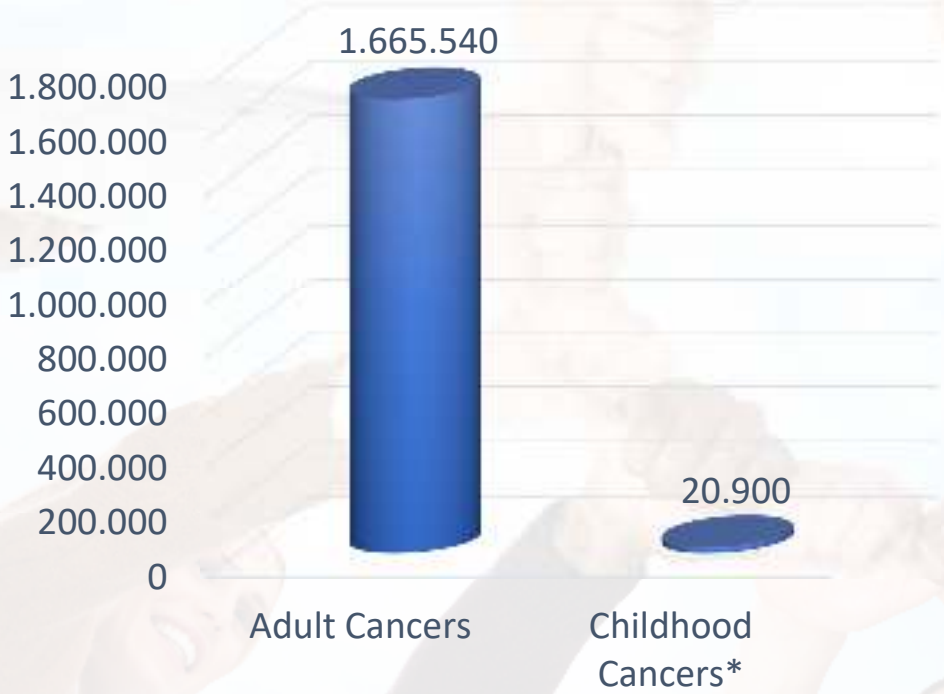
# Disclosure

- I am an employee and have an investment interest in Sanofi
- Certain components of this lecture were originally presented at the Accelerate Conference in 2017

# Cancer in the US



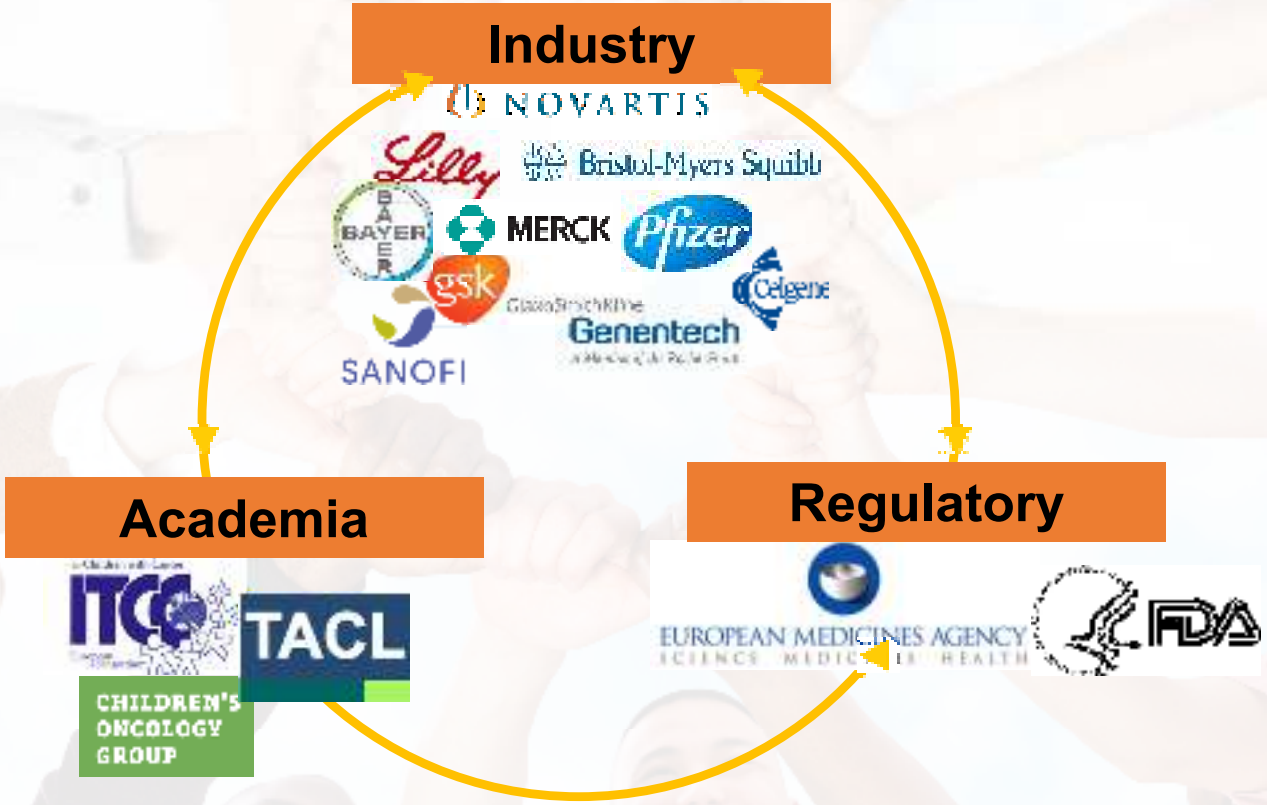

- Cancer is the leading cause of death from disease in children
- One in every 330 Americans develops cancer before age 20
- 1 in 750 20-year-olds alive in the U.S. today is a survivor of childhood cancer.
- More than half of survivors have serious, life-long consequences of treatment

* 0 – 19 years of age

# The challenge

- Improve cure rates
- Diminish acute toxicity
- Minimize risk for late effects

# Pediatric Drug Development




Originally presented at Accelerate Conference 2017 – Peter Adamson

# Pediatric Drug Development: Regulatory Initiatives

- Best Pharmaceuticals for Children's Act (BPCA)
  - Voluntary incentive (extension of exclusivity)
- Pediatric Research Equity Act (PREA)
  - Required but historically most oncology drugs received waivers
- Research to Accelerate Cures and Equity (RACE) for Children Act
  - Now fully enacted
  - Based on relevance of drug target to childhood cancer(s)
  - Minimizes waivers
- EMA: Paediatric Investigational Plans (PIPs)

# Pediatric Drug Development: Regulatory Initiatives

- Have catalyzed discussion between stakeholders, especially academic childhood cancer networks and industry partners
- Early pediatric regulatory initiatives had relatively limited impact for children with cancer
- Full impact of RACE (2021) to be determined

European Journal of Cancer 112 (2019) 49–56

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

# Timing of first-in-child trials of FDA-approved oncology drugs

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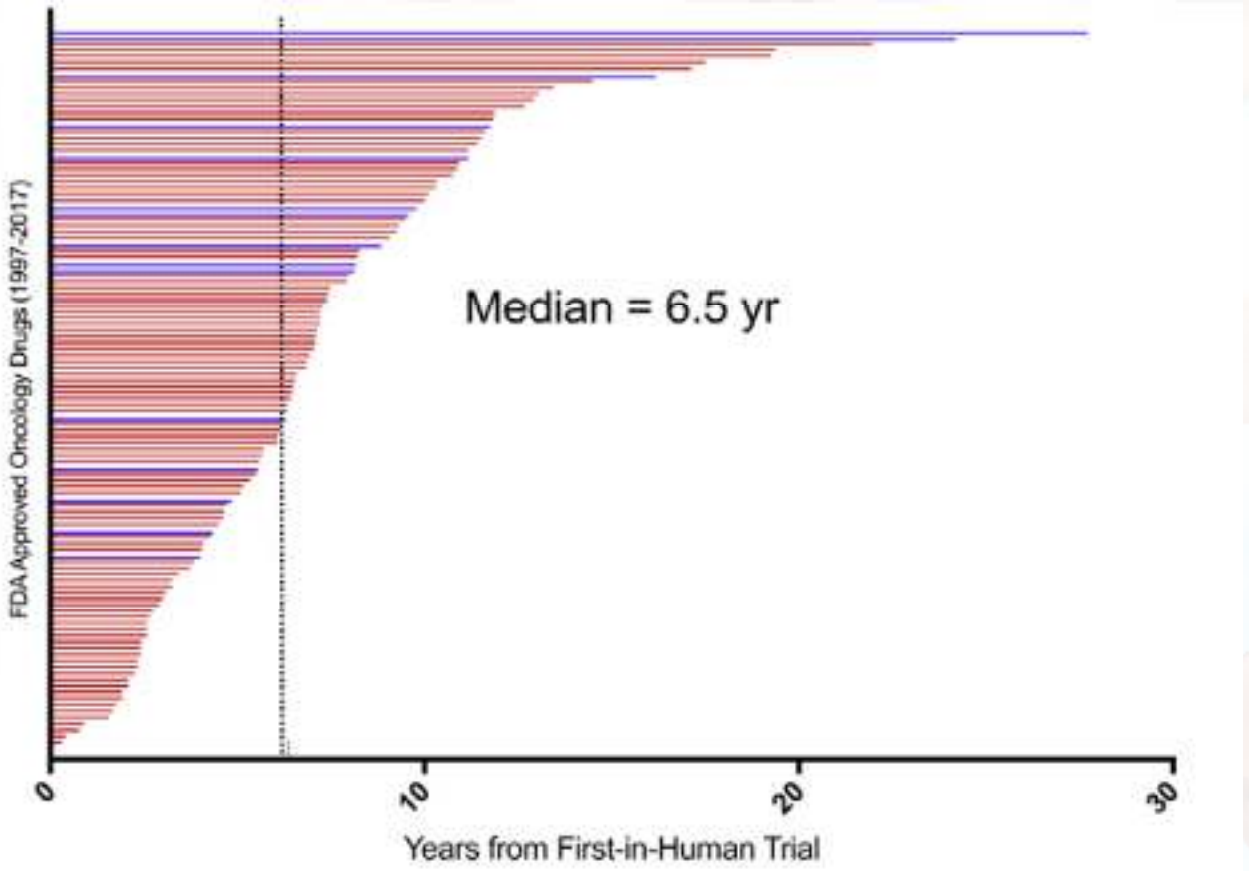
**KEYWORDS**
Paediatric cancer;
Phase 1 trials;
Drug development;
Targeted therapy;
Disparity

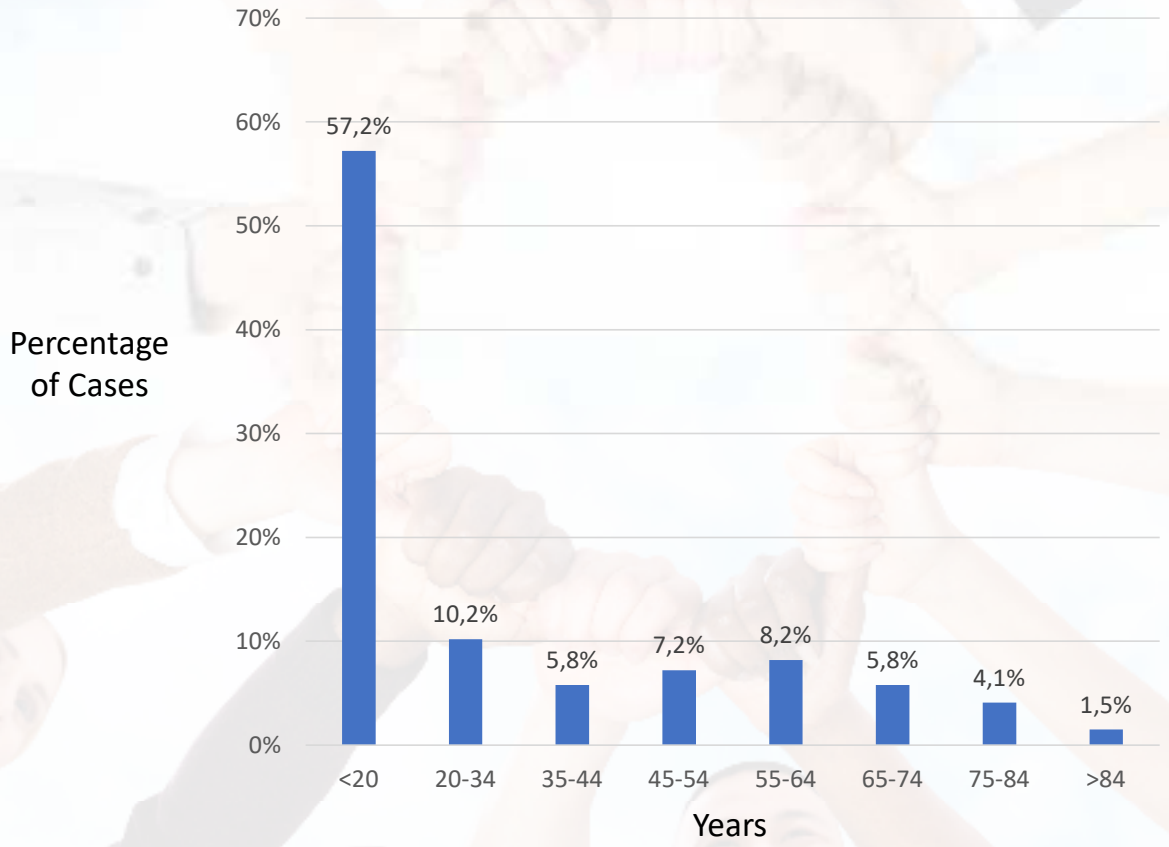
**Abstract** *Aim:* The lag time between initial human studies of oncology agents and the first-in-child clinical trials of these agents has not been defined.
*Methods:* We conducted a systematic analysis of time from first-in-human trials to first-in-child trials (age of eligibility <18 years) of agents first approved by the US Food and Drug Administration (FDA) for any oncology indication from 1997 to 2017. We used clinical trial registry data, published literature and oncology abstracts to identify relevant trials and start dates.
*Results:* From 1997 to 2017, 126 drugs received initial FDA approval for an oncology indica-

# Time between the start date of first-in-human clinical trial and first trial eligible to enroll paediatric patients




Neel et al, 2019 European J Cancer

# New Cases of Acute Lymphoblastic Leukemia by Age Group




SEER 18; 2009-2013

# Pediatric Development: Novel drug for ALL

- First presentation of efficacy in adults presented in 2011
- Drug was approved for adults with relapsed ALL in 2017
- First child enrolled in a pediatric study was also in 2017

How did we arrive at a point where a new drug reached regulatory approval for adult ALL and pediatric clinical trials were just starting?

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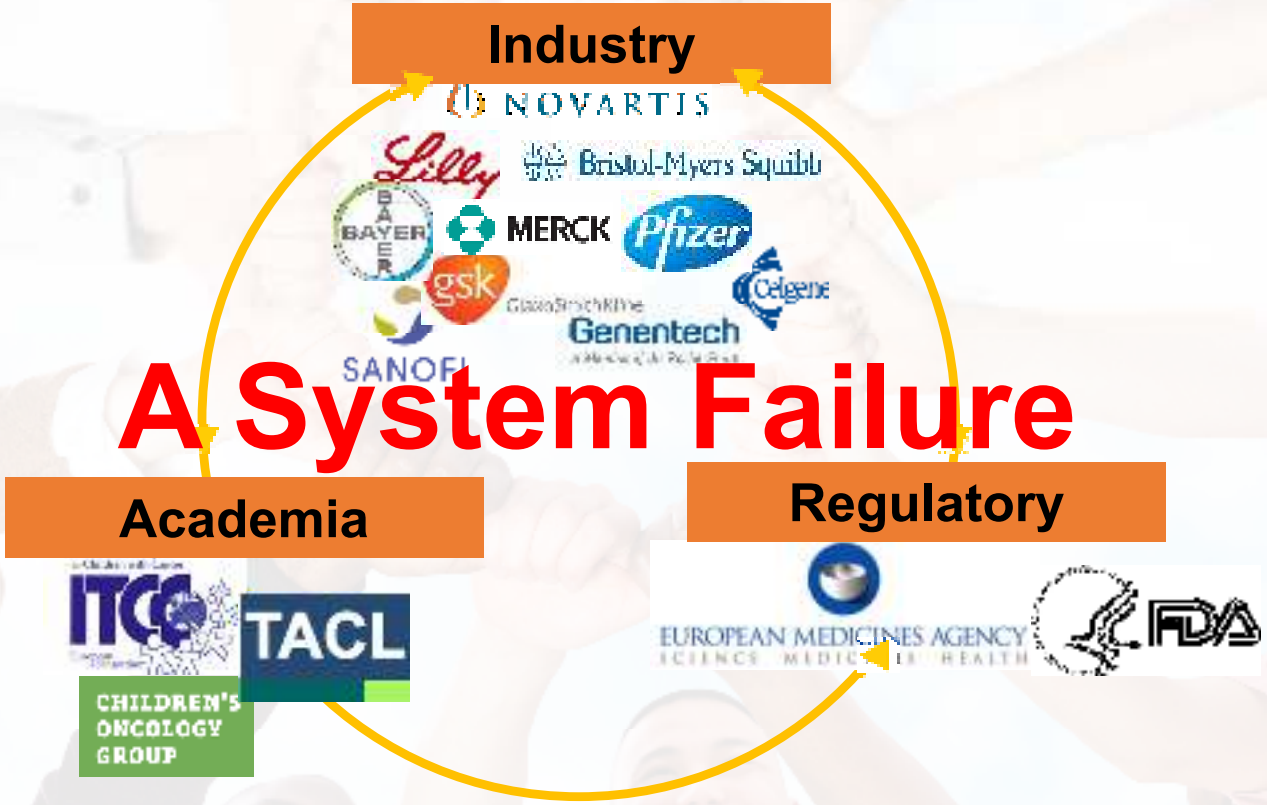
# Pediatric Drug Development

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# A System Failure: Industry*

- Does not want to invest significant resources in pediatric development until there is a reasonable likelihood of regulatory approval for an adult indication

- In many circumstances, seeks to minimize its financial investment in pediatric development

* Generalizations -- there will be exceptions

# A System Failure: Academia

- Should there be a more robust push to get into the clinic faster?
- Should we start with simpler trial designs?
- Can the efficiency of study development be improved?

# A System Failure: Regulatory Agencies

- Are requirements too granular or restrictive?

- Should pediatric oncology have a *greater* regulatory burden than medical oncology?
  - For example: Requirement to define optimum biologic dose *vs* safe and effective dose

# Progress

- Regulatory Incentives & Requirements
  - Major catalyst throughout industry to build pediatric capabilities
  - RACE implementation furthering drive for improvements in capability
- Cluster Meetings between FDA and EMA
  - Leading to better informed plans
- PIPs & Pediatric Plans improving over time
- Childhood cancer drug development is on the radar screen

ACCELERATE

INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

An international multistakeholder organization to

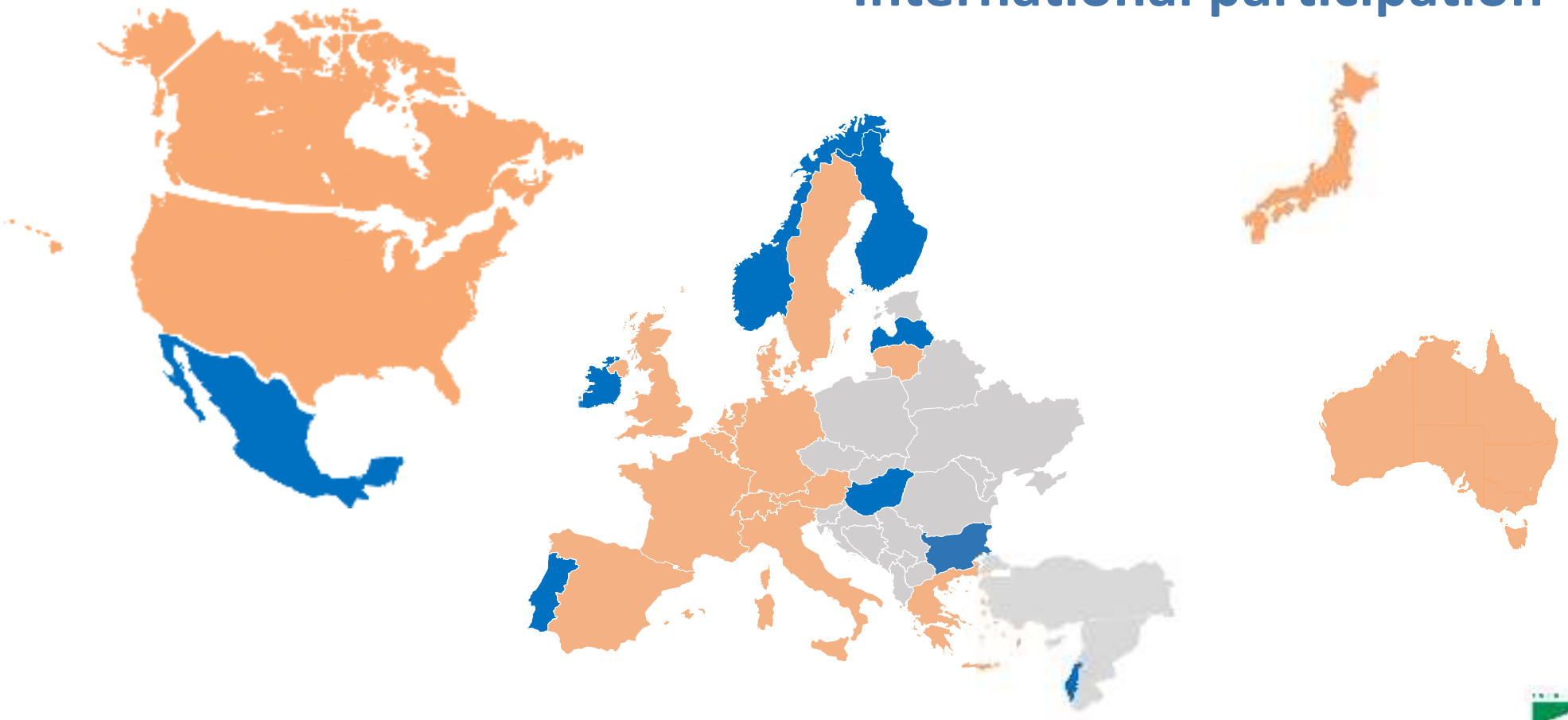
# Improve and accelerate new drug development for children and adolescents with cancer

A patient centric organisation to solve problems

Created in 2015

FOUNDATION

# International participation



Already present in 2020

New entries

EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

FDA U.S. FOOD & DRUG ADMINISTRATION

# Paediatric Strategy Forums
## Continually evolving


Andy Pearson

**2017**
- PSF - 1 **ALK inhibition**
- PSF - 2 **Mature B-cell lymphoma**

**2018**
- PSF - 3 **CheckPoint Inhibitors**

**2019**
- PSF - 4 **Acute Myeloid Leukemia**
- PSF Prioritisation **Acute Myeloid Leukemia**

**2020**
- PSF - 5 **Epigenetic modifiers**
- PSF Prioritisation **BET inhibitors**

**2021**
- PSF - 6 **Second ALK inhibition**
- PSF - 7 **CAR T cells**
- PSF - 8 **TKI in Sarcomas**

**2022**
- PSF - 9 **RAF and MEK inhibitors**
- PSF - 10 **To be decided**
- PSF - 11 **To be decided**


FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs: Amendments to Sec. 505B of the FD&C Act
Guidance for Industry

# Progress (but)

- Little evidence that we are shortening the timeline between FIH studies and First in Children studies

- **In general, a maximum of two phase 3 trials in any given pediatric cancer can be conducted globally every 4-6 years**
  - Prioritization should be considered by all stakeholders to allow more rapid development of high priority drugs
  - Discussions about a phase 3 trials design prior to any pediatric clinical data being available are resource draining and counterproductive

# Path Forward

- The clinical development of *high priority new agents* can be accelerated
- Regulatory *incentives* and *requirements* should be better aligned to meet the goal of expeditiously moving *high priority new agents* into pediatric clinical development