# Improved access to new drugs for children and adolescents with cancer: ACCELERATE

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

23 June 2022

Summer Conference of AKEK 23

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- What is ACCELERATE
- Working Groups
- Paediatric Strategy Forums
- Future

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ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

**An international multi-stakeholder organization to**
**Improve and accelerate new drug development**
**for children and adolescents with cancer**

A patient centric organisation to solve problems

Created in 2015

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# Strategy

## Principles

- Identify a problem together (annual conference)
- Understand the issue in an open multi-stakeholder dialogue
- No blame ! No shame!
- Generate data
- Find solutions
- Implement solutions

European Journal of Cancer 166 (2022) 145–164

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

ELSEVIER

EJC

Review

ACCELERATE – Five years accelerating cancer drug development for children and adolescents

Andrew D.J. Pearson [a,*], Susan L. Weiner [b], Peter C. Adamson [c], Dominik Karres [d], Gregory Reaman [e], Raphaël Rousseau [f], Patricia Blanc [g], Koen Norga [h], Jeffrey Skolnik [i], Pam Kearns [j], Nicole Scobie [k], Elly Barry [l], Lynley V. Marshall [m], Leona Knox [n], Hubert Caron [o], Darshan Wariabharaj [p], Alberto Pappo [q], Steven G. DuBois [r], Lia Gore [s], Mark Kieran [l], Brenda Weigel [t], Elizabeth Fox [q], Karsten Nysom [u], Teresa de Rojas [a], Gilles Vassal [a,v]

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# We need new drugs for children with cancer…
# BUT: Current paradox

## ADULTS

- Many new drugs in development
- These drugs become therapies for children

↓

- Waived or delayed pediatric developments
- Poor access to pediatric patients

## CHILDREN

Rare population (small N)

↓

**Little commercial interest**
**Poor access to innovation**

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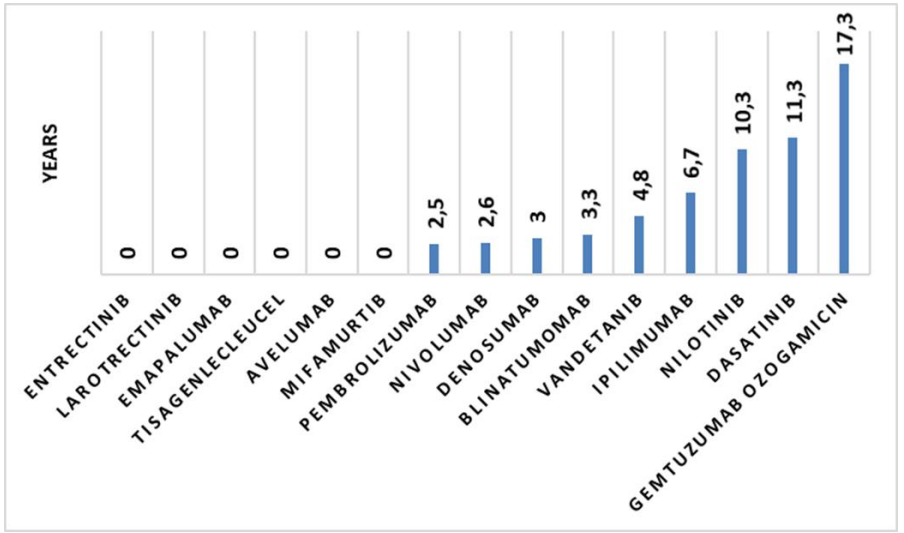
# Strategy

## Challenges

Important changes needed to accelerate development of new medicines

- Development of anti-cancer medicines for children should be driven by an agent's mechanism of action, rather than by its adult condition
- New drugs with high potential for benefit must be quickly assessed and evaluated in children and adolescents - delay currently (median 6.5 years) first-in-human trials to the start of first-in-child trials




28 of 169 (16.6%) approved anticancer medicines paediatric indication
None for CNS tumours, Ewings sarcoma, rhabdomyosarcoma.
One neuroblastoma

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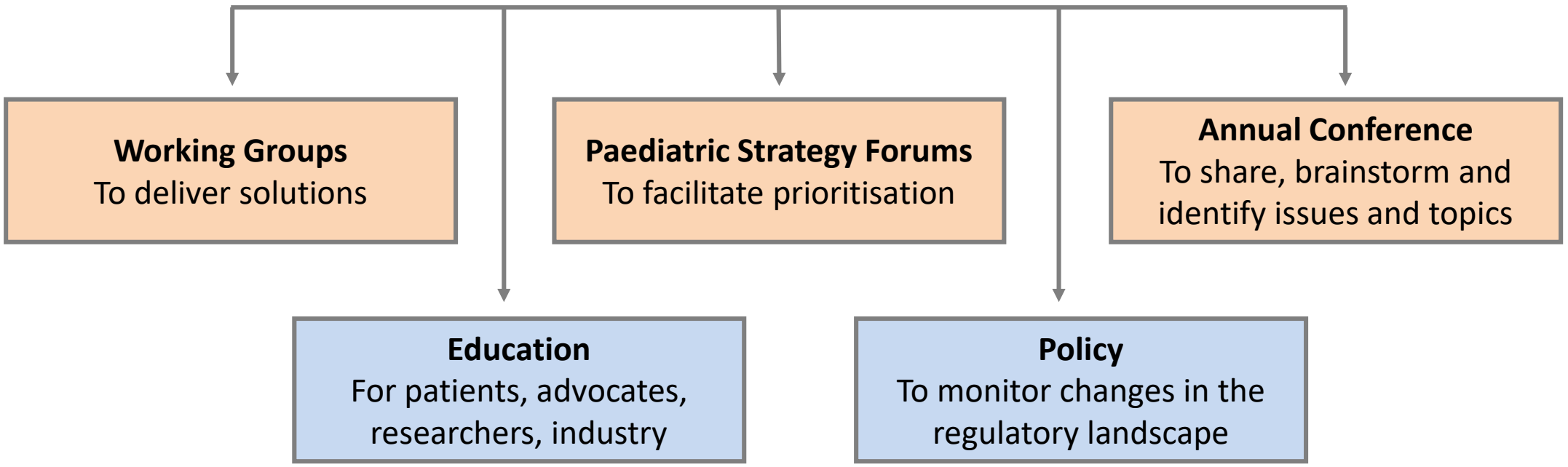

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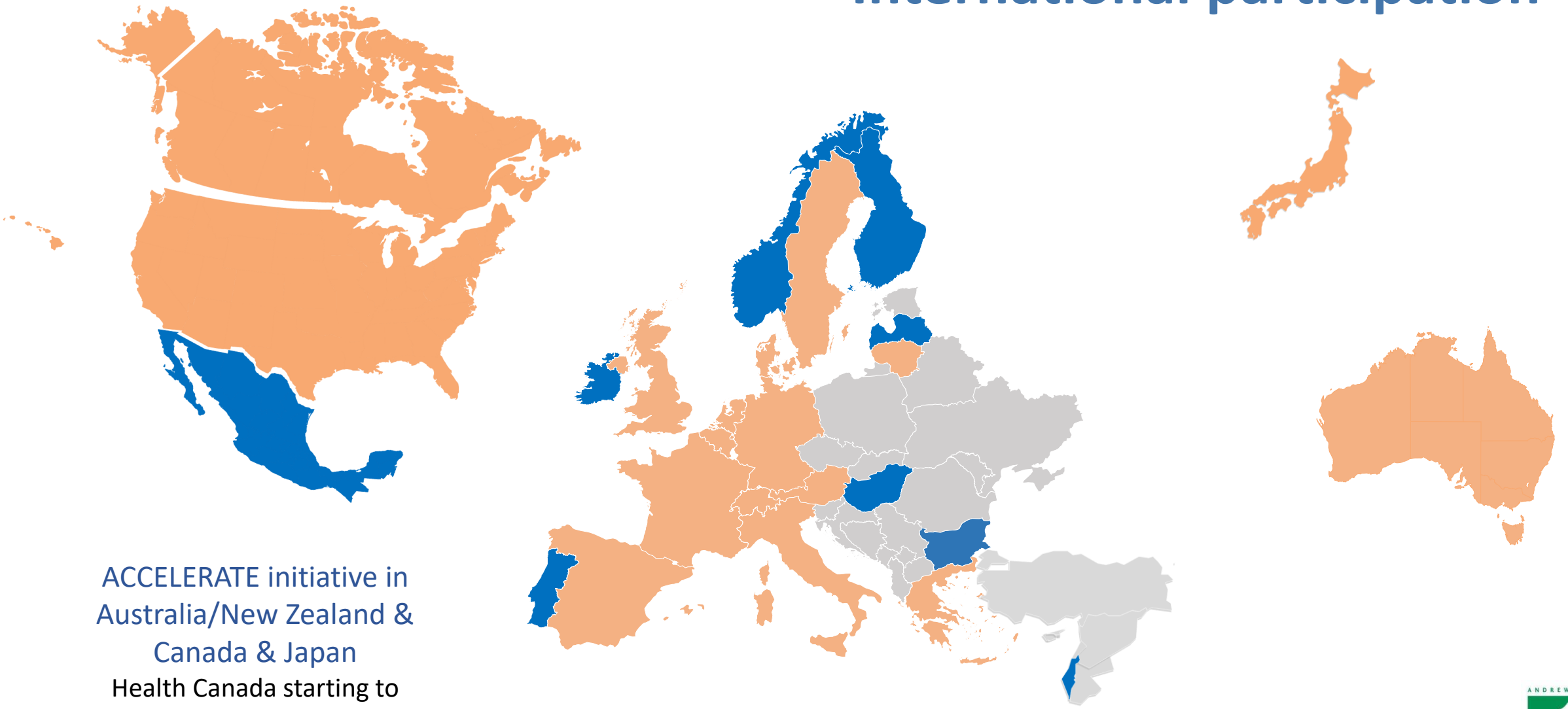
# International participation



ACCELERATE initiative in Australia/New Zealand & Canada & Japan

Health Canada starting to work on paediatric regulations

Already present in 2020

New entries

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# ACCELERATE Steering Committee

## Academia


Steven DuBois


Pam Kearns


Lynley Marshall


Lia Gore

## Industry


Elly Barrv


Hubert Caron


Heather Wasserstrom


Darshan Wariabharaj

## Patients Advocacy


Leona Knox


Patricia Blanc


Susan Weiner


Nicole Scobie

## Regulatory Bodies


Koen Norga


Dominik Karres


Gregory Reaman


Alberto Pappo

## Intuitu personae


Jeffrey Skolnik


Raphael Rousseau


Peter Adamson

## SIOP Europe CEO


Samira Essiaf

## ITCC President / ACCELERATE Chair


Gilles Vassal

## PSF Oversight Committee Chair/Senior Advisor


Andy Pearson

### ACCELERATE Team


**Andrea Demadonna**
ACCELERATE Coordinator


**Teresa de Rojas**
Scientific Coordinator


**Beatriz Martinez**
Comm/Marketing Coordinator

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- What is ACCELERATE
- **Working Groups**
- Paediatric Strategy Forums
- Future

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# Ongoing Multi-stakeholder Working Groups

Analyse specific paediatric oncology challenges and propose solutions

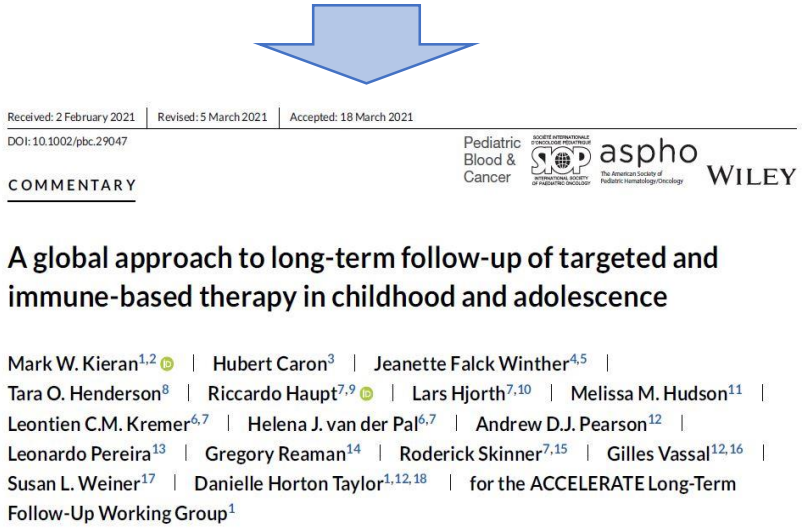
**Fostering Age Inclusive Research**

**Fit For Filing**

**Long Term Follow Up**

**International Collaboration**

**Real World Evidence**



Received: 2 February 2021 | Revised: 5 March 2021 | Accepted: 18 March 2021

DOI: 10.1002/pbc.29047

Pediatric Blood & Cancer | aspho | WILEY

COMMENTARY

## A global approach to long-term follow-up of targeted and immune-based therapy in childhood and adolescence

Mark W. Kieran[1,2] | Hubert Caron[3] | Jeanette Falck Winther[4,5] | Tara O. Henderson[8] | Riccardo Haupt[7,9] | Lars Hjorth[7,10] | Melissa M. Hudson[11] | Leontien C.M. Kremer[6,7] | Helena J. van der Pal[6,7] | Andrew D.J. Pearson[12] | Leonardo Pereira[13] | Gregory Reaman[14] | Roderick Skinner[7,15] | Gilles Vassal[12,16] | Susan L. Weiner[17] | Danielle Horton Taylor[1,12,18] | for the ACCELERATE Long-Term Follow-Up Working Group[1]

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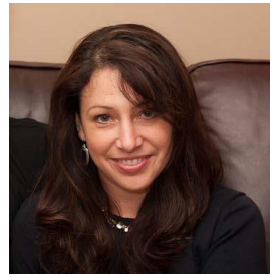
# ACCELERATE

## Fit for Filing

## Co-chairs Pam Kearns & Elly Barry



- Aim to develop best principles to design and deliver an academic clinical trial with a dataset that meets the expectations for inclusion in a regulatory package.
- Ultimately improve the implementation of investigator-initiated-trials in an intent to file

**Major Value to all clinical trials group including ITCC**


### Output

**Consensus manuscript (JCO in Press)**
**Educational strategy**

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# ACCELERATE

## International Collaboration

## Co-chairs

## Teresa de Rojas, Nicole Scobie & Greg Reaman

| | |
|---|---|
| Identify | Identify the real obstacles to international cooperation and collaboration |
| Develop | Develop principles and best practices for global clinical research in the US-EU-UK-Canada-JAPAN to enable pediatric oncology focused cooperative groups and clinical trial centers to collaborate to ACCELERATE drug development |
| Synergy | Provide synergy, but not overlap, with other WGs (e.g. Fit-for-Filing) and ITCC Sponsor Committee |

- ✓WP-1 Systematic review of international clinical trials
- ✓WP-2 Data survey of intercontinental trials
- WP-3 Multi-stakeholder discussion and consensus

Received: 11 August 2021 | Revised: 21 September 2021 | Accepted: 21 September 2021

DOI: 10.1002/cam4.4356

RESEARCH ARTICLE

Cancer Medicine Open Access WILEY

### Intercontinental collaboration in clinical trials for children and adolescents with cancer—A systematic review by ACCELERATE

Teresa de Rojas[1] | Andrew J. Pearson[1] | Nicole Scobie[2] | Leona Knox[3] | Darshan Wariabharaj[4] | Pamela Kearns[5] | Gilles Vassal[1,6] | Gregory Reaman[7]

- 25% late phase - academia COG -US-Oceania
- Majority industry early phase (North-America and Europe, **less involvement** of Oceania or Asia.

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- What is ACCELERATE
- Working Groups
- ➢ **Paediatric Strategy Forums**
- Future

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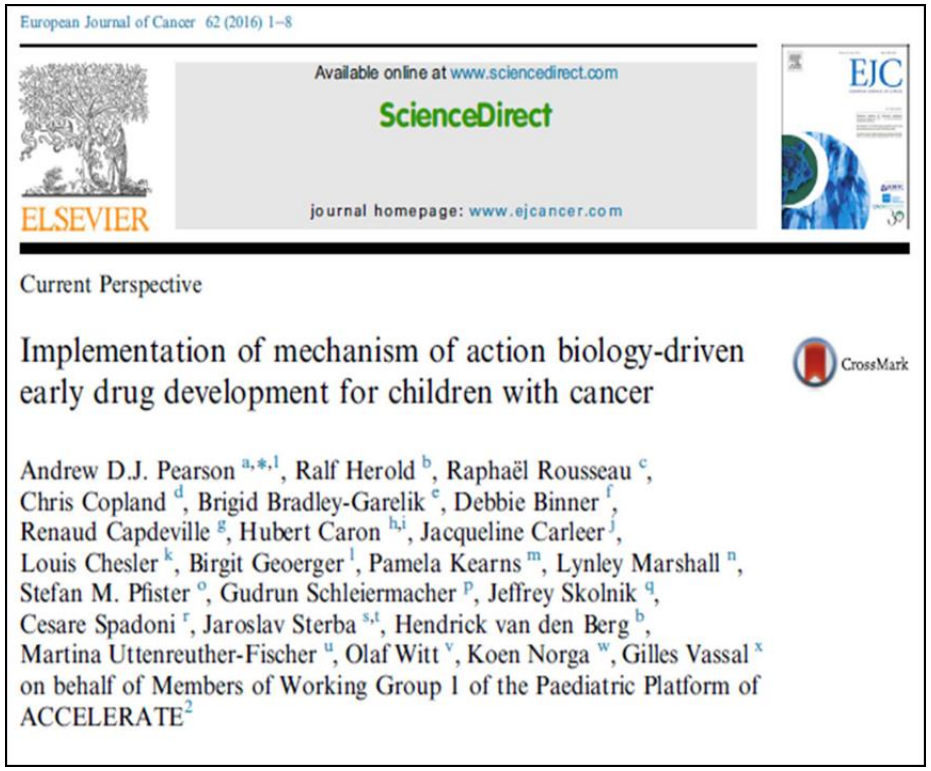
SCIENCE MEDICINES HEALTH

FDA U.S. FOOD & DRUG ADMINISTRATION

# New drug development strategy



European Journal of Cancer 62 (2016) 1–8

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

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Current Perspective

Implementation of mechanism of action biology-driven early drug development for children with cancer

CrossMark

Andrew D.J. Pearson [a,*,1], Ralf Herold [b], Raphaël Rousseau [c], Chris Copland [d], Brigid Bradley-Garelik [e], Debbie Binner [f], Renaud Capdeville [g], Hubert Caron [h,i], Jacqueline Carleer [j], Louis Chesler [k], Birgit Geoerger [l], Pamela Kearns [m], Lynley Marshall [n], Stefan M. Pfister [o], Gudrun Schleiermacher [p], Jeffrey Skolnik [q], Cesare Spadoni [r], Jaroslav Sterba [s,t], Hendrick van den Berg [b], Martina Uttenreuther-Fischer [u], Olaf Witt [v], Koen Norga [w], Gilles Vassal [x] on behalf of Members of Working Group 1 of the Paediatric Platform of ACCELERATE[2]

## Mechanism of action biology-driven early drug development

- Aggregated database of paediatric biological tumour drug targets
- Joint academic–pharmaceutical industry pre-clinical platform to analyse the activity of new drugs (ITCC-P4) - ongoing IMI2 project
- ➢ **Paediatric Strategy Forums to facilitate prioritisation**
- Molecular profiling of paediatric tumours at diagnosis and relapse

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# Paediatric Strategy Forums

- **Accelerate drug development**
- ***Share*** information between all stakeholders and ***inform*** paediatric drug development strategies and *subsequent* decisions
- Improve the **selection *and prioritisation*** of innovative drugs being evaluated for children and adolescents cancer -driven by science and meet patients' unmet needs
- Global involvement


**Multi-stakeholder**
Clinicians, industry, regulators, patient advocates
**Equal partners**

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FDA U.S. FOOD & DRUG ADMINISTRATION

# Paediatric Strategy Forums

## Continually evolving

### 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
**MAPK inhibitors**

PSF -10
**DNA Damaging agents**

### 2023

PSF - 11
**PI3K/AKT/mTOR Pathway**

PSF - 12
**CDK 4, 6 & 9 inhibitors**

PSF - 13
**Topic To be decided**

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# Paediatric Strategy Forums

European Journal of Cancer xxx (xxxx) xxx

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

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Review

Paediatric Strategy Forum for medicinal product development of chimeric antigen receptor T-cells in children and adolescents with cancer ACCELERATE in collaboration with the European Medicines Agency with participation of the Food and Drug Administration[2]

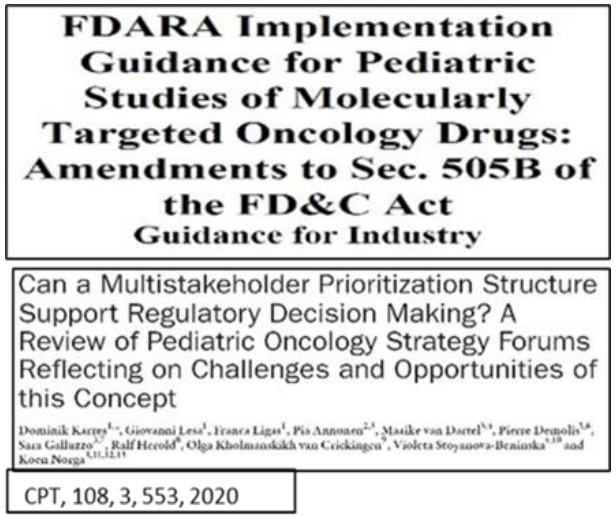
Andrew DJ. Pearson [a,*,1], Claudia Rossig [b,1], Crystal Mackall [c,1], Nirali N. Shah [d,1], Andre Baruchel [e,1], Gregory Reaman [f], Rosanna Ricafort [g], Delphine Heenen [h], Abraham Bassan [i], Michael Berntgen [j], Nick Bird [k], Eric Bleickardt [l], Najat Bouchkouj [f], Peter Bross [f], Carrie Brownstein [m], Sarah Beaussant Cohen [n], Teresa de Rojas [a], Lori Ehrlich [f], Elizabeth Fox [o], Stephen Gottschalk [o], Linda Hanssens [p], Douglas S. Hawkins [q], Ivan D. Horak [r], Danielle H. Taylor [s], Courtney Johnson [f], Dominik Karres [t], Franca Ligas [t], Donna Ludwinski [u], Maksim Mamonkin [v], Lynley Marshall [w], Behzad K. Masouleh [x], Yousif Matloub [y], Shannon Maude [z], Joe McDonough [aa], Veronique Minard-Colin [ab], Koen Norga [ac], Karsten Nysom [ad], Alberto Pappo [o], Laura Pearce [ae], Rob Pieters [af], Martin Pule [ag], Alfonso Quintás-Cardama [ah], Nick Richardson [f], Martina Schüßler-Lenz [ai,as], Nicole Scobie [aj], Martina A. Sersch [ak], Malcolm A. Smith [al], Jaroslav Sterba [am], Sarah K. Tasian [z], Brenda Weigel [an], Susan L. Weiner [ao], Christian Michel Zwaan [af,ap,ar], Giovanni Lesa [t], Gilles Vassal [a,aq]

## Paediatric Strategy Forum for Medicinal Product Development of CAR T-cells in children

- 236 Participants
- Europe, US, Canada, China, Singapore, Australia
- 13 Companies
- Academia – 107, Patient Advocates – 14, Industry – 54, - Regulators - 43 – EMA; FDA; HTA; MHRA; Heath Canada

**Clear Conclusions**

# Paediatric Strategy Forums




- Living" prioritisation mTKI in Bone Sarcomas
- **Continually developing and adapting to needs**

## General principles

- Global academic collaboration
- **Early** academia-multi company engagement
- **Early** engagement with regulators
- **Multiple products of the same class - Focused and sequential development**
- Platform trials
- Very rare malignancies with same biology in adults - development & regulatory pathway - children, adolescents and adults

# Paediatric Strategy Forums

## Output

- Prioritisation of  classes of drugs e.g combination checkpoint inhibitors
- Prioritisation of products e.g. menin inhibitors
- PedAL/EUPAL, GloBNHL Platform Trials
- European – North America collaboration
- Rapid publications -6 months

European Journal of Cancer 127 (2020) 52–66

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

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Original Research

ACCELERATE and European Medicines Agency Paediatric Strategy Forum for medicinal product development of checkpoint inhibitors for use in combination therapy in paediatric patients

Andrew D.J. Pearson [a,*], Claudia Rossig [b], Giovanni Lesa [c], Scott J. Diede [d], Susan Weiner [e], John Anderson [f], Juliet Gray [g], Birgit Geoerger [h], Veronique Minard-Colin [h], Lynley V. Marshall [i], Malcolm Smith [j], Paul Sondel [k], Marcis Bajars [l], Claudia Baldazzi [m], Elly Barry [n], Sam Blackman [a], Patricia Blanc [o], Renaud Capdeville [p], Hubert Caron [q], Peter D. Cole [r], Jorge Camarero Jiménez [s], Pierre Demolis [t], Martha Donoghue [u], Mabrouck Elgadi [v], Thomas Gajewski [w], Sara Galluzzo [x], Robert Ilaria Jr [y], Alessandro Jenkner [z], Dominik Karres [c], Mark Kieran [aa], Franca Ligas [c], Israel Lowy [ab], Michael Meyers [ac], Corina Oprea [ad], Vijay G.R. Peddareddigari [ae], Jaroslav Sterba [af], Paul K. Stockman [ag], Peter Suenaert [ah], Uri Tabori [ai], Cornelis van Tilburg [aj], Todd Yancey [ak], Brenda Weigel [al], Koenraad Norga [am], Gregory Reaman [u], Gilles Vassal [h]

# Evaluation of Impact of Paediatric Strategy Forums

- 53%  industry attendees stated that the Forum resulted in change in the company's decisions
- PIP or Written Request - 62% high-priority assets; 5% not considered high priority
- B-cell Forums - increase in waivers for non-prioritised B cell products
- Checkpoint  Forum – focus on combination, not monotherapy

| Time Period | Scientifically Justified Waivers – B-cell | Monotherapy trials part of PIP – Checkpoint |
|---|---|---|
| Before Forum | 44% | 67% |
| After Forum | 75% | 6% |

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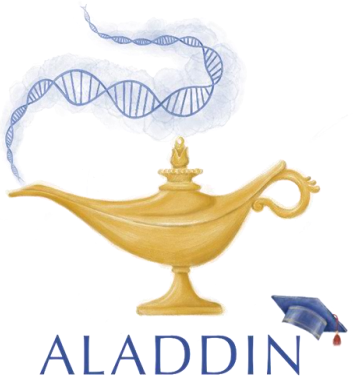
# ALADDIN

## Multi-stakeholder Education Alliance to Accelerate Drug Development for Children and Adolescent with Cancer

- Course Strategic/ Regulatory Science
- 360º Multi-stakeholder Rotation
- ACCELERATE Research Fellowship
- Online Educational Training Program

Fit for Filling Webinars

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# Breakout sessions at 2022 ACCELERATE Conference

- Optimising Industry/Academia partnerships → Workshop on platform trials
- Innovation after a first pediatric regulatory approval → Manuscript on innovation after approval
- When is a Randomized Clinical Trial not required for registration→ Facilitating RWE project as proof of concept

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# Future directions

- Increase the number of “relevant” innovative drugs
- Improve the selection and prioritisation of innovative drugs
- Accelerate evaluation and introduction of innovative drugs into front-line therapy
- Improve access
- Align HTAs in paediatric drug development process
- Lobby regarding the new EU regulatory environment

European Commission

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European Medicines Agency and European Commission (DG Health and Food Safety) action plan on paediatrics

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# Conclusion

## Great value – international multi-stakeholder with critical role of advocates

- Enhanced communication and understanding between academia, industry, patient advocates and regulators.
- Promoted mechanism-of-action driven approach
- Developed Paediatric Strategy Forums - prioritisation of medicinal products
- Strongly supported alignment between the EMA and the US FDA
- Identification of unmet medical needs through multi-stakeholder collaboration
- Championed early assessment of promising drugs in adolescents

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