Overview: Pediatric Landscape Analysis, Industry Perspective

FDA ADEPT 9 Public Meeting
Diversity in Clinical Trials
September 6, 2024

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Disclaimer

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Acknowledgements

Many thanks to my data partners who provide access to the proprietary database sources that support the customized analyses in this presentation:

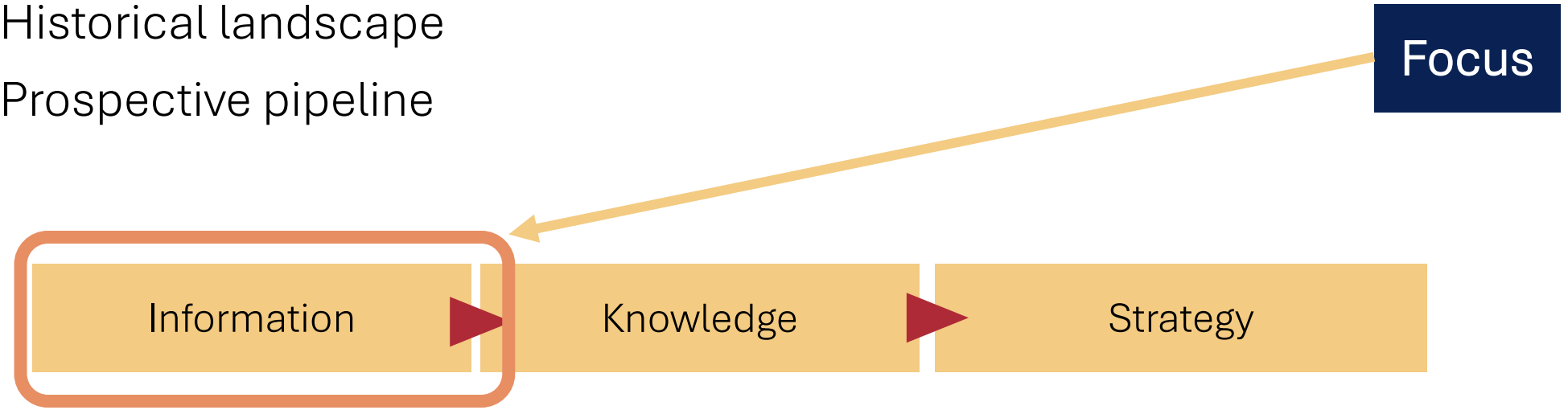
- ***Marija Jukic*, *Vice President, IPD Analytics***
- ***Sean Crowley*, *Vice President, Evaluate Pharma and Citeline***

Agenda

1. Overview of Historical Industry-Sponsored Pediatric Clinical Trial Landscape
2. Case Studies: Ulcerative Colitis & Asthma
3. Observations Unique to Industry-Sponsored Pediatric Clinical Trials
4. Overview of Prospective Pipeline for Pediatrics
5. Summary

Impetus for this Pediatric Landscape Analysis

- There is a keen interest in improving pediatric product development globally
- Strategies for improving diversity in clinical trials will benefit from this context
- However, there are no pediatric-specific comprehensive analyses of:
  1. Historical landscape
  2. Prospective pipeline



The goal of this session is to provide foundational information to set the context for building our knowledge and formulating strategies, including those impacting diversity.

Pediatric Product Development

1. **Historical characterization of industry-sponsored pediatric clinical trials**
2. Prospective view of upcoming industry-sponsored pediatric clinical trials

Approach: Historical Landscape

15-Year Historical Analysis of Industry-Sponsored Pediatric Clinical Trials (2009-2024)

Created a comprehensive, customized global landscape dataset (proprietary databases and public data)

Inclusion Criteria:

Ages	Birth to 18 years
Phases	Phases 1 to 4
Status	Active or Completed
Indications	All
Countries	All
Sponsors	Industry or Industry plus collaborators [1]
Modalities	Drugs, Biologics, Gene and Cell therapies
Study Objective	PK, PD, Safety, Efficacy
Study Design	Interventional

Result:

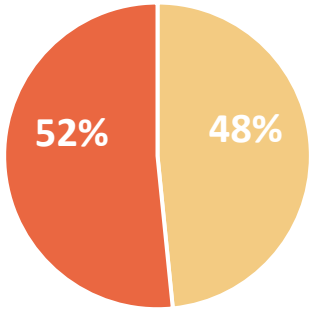
2,500 Industry-sponsored pediatric clinical trials

Aim: Generate data to support new PRODUCT DEVELOPMENT

1 collaborators are government, academia and cooperative networks

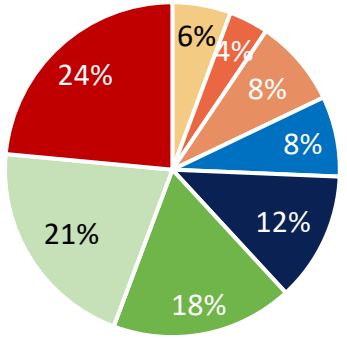
Characterization: Who, What and How…

By Sponsor Type



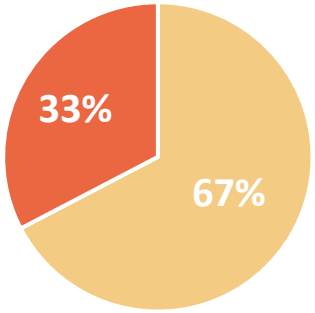
Top 20 Pharma Mid-sized and Biotech

By Therapeutic Area



- Cardiovascular
- Oncology
- Infectious Disease
- Other
- Metabolic/Endocrinology
- Autoimmune/Inflammation
- CNS
- Vaccines

Required by Legislation vs. Not



Not Required Required

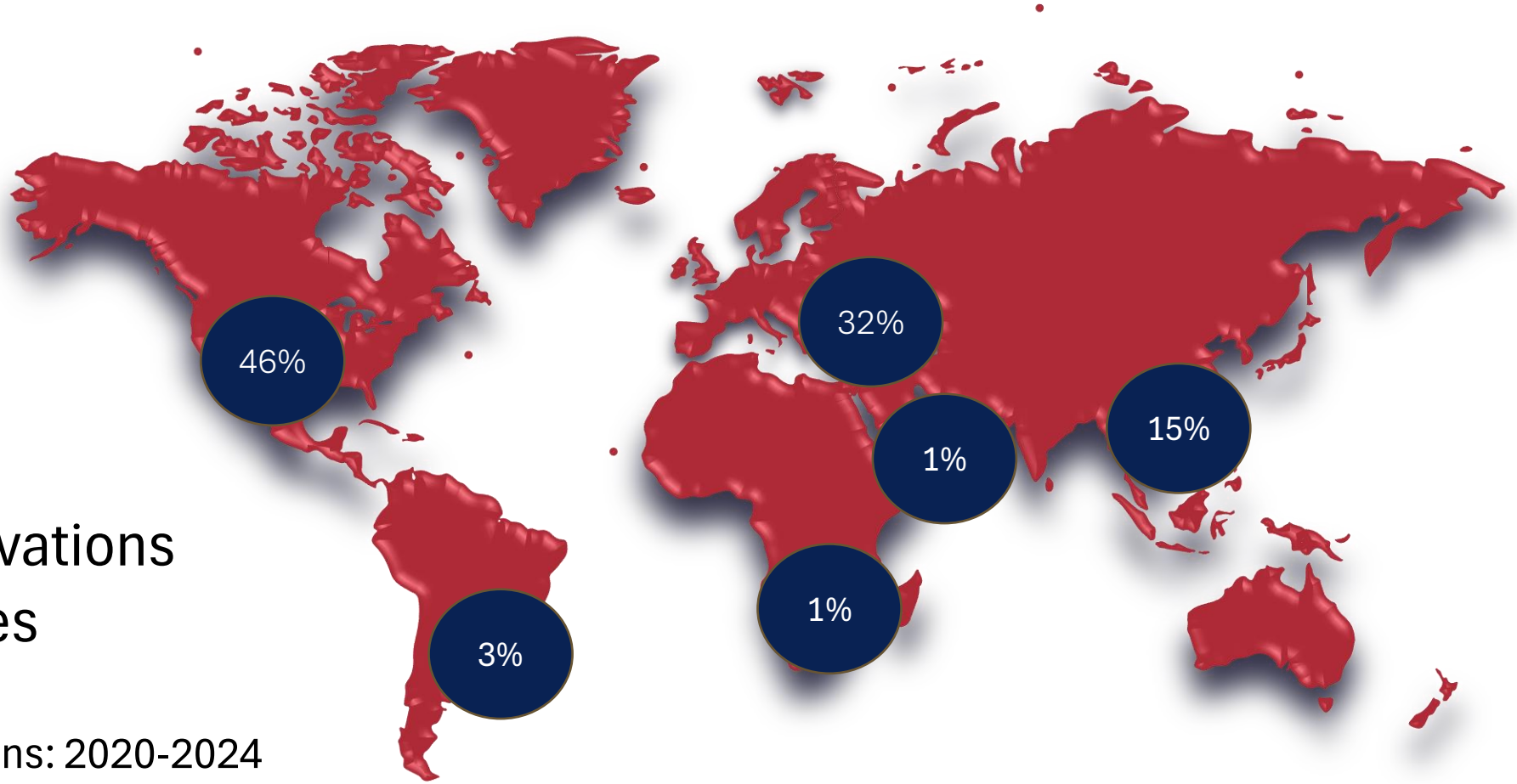
Median Size and Scope (excluding vaccines)

Phases II and III

- **120** Patients per Trial
- **23** Sites per Trial
- **2** Patients per Site per Year
- **4** Countries per Trial

Notes: N = 2,500 pediatric clinical trials for all graphs. In the "Required vs. Not" chart, the "Required" may include both PREA+BPCA and PREA alone. For the Median Size and Scope box, N = 1,136 industry-sponsored pediatric clinical trials
Source: Mezzopointe, LLC customized analysis: 15-Year Historical Overview (2009-2024); N = 2,500 Pediatric Clinical Trials. Primary data sources: Evaluate Pharma, Trial Trove and IPD Analytics, accessed July 2024.

Global Characterization: Where…



- 52k site activations
- 113 countries

Recent Site Activations: 2020-2024

Russia, Ukraine and Turkey stopped	China, South Korea, Argentina and Canada significantly increased	South Africa and India significantly decreased

Source: Mezzopointe, LLC customized analysis: 15-Year Historical Overview (2009-2024); N = 2,500 Pediatric Clinical Trials. Primary data sources: Evaluate Pharma, Trial Trove and IPD Analytics, accessed July 2024.

Country Enrollment in Perspective

Pediatric study populations are relatively small, and patients are dispersed across the world

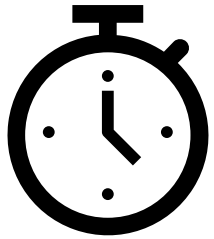
Example to illustrate # patients per country

TA Example	Prevalence in children	# Enroll	#Countries	Patients/ Site	Patients/ Country
Oncology N = 60	Very Low	70	7	3	10

In comparison, adult oncology trials will enroll **15x** these #s by country.

Source: Mezzopointe, LLC customized analysis: 15-Year Historical Overview (2009-2024); N = 2,500 Pediatric Clinical Trials. Primary data sources: Evaluate Pharma, Trial Trove and IPD Analytics, accessed July 2024
Medians. Phase II and III pediatric clinical trials

Characterization: When…



Long timelines are often cited as a major concern for all – patients, caregivers, clinicians, researchers, sponsors & regulators

Initial Product Approval

9-year gap between adult approval and most pediatric label changes [1]

8 years to complete pediatric programs and achieve pediatric label changes (end-to-end time) [2]

Pediatric Label Change

1. Analysis completed by J&J in 2016. Based on FDA approval database.
2. Mezzopointe, LLC customized analysis: 15-Year Historical Overview (2009-2024); N = 2,500 Pediatric Clinical Trials. Primary data sources: Evaluate Pharma, Trial Trove and IPD Analytics, accessed July 2024.

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Pediatric Clinical Trials: End-to-End Time

Over the 15-year period, there was no observed shortening of time to complete pediatric programs

Pediatric Clinical Trial End-to-End Years to Complete

8 Years

Examples at Indication Level	Years
Type 2 Diabetes	12
Pulmonary Arterial Hypertension (PAH)	11
Ulcerative Colitis	9

Recent changes in landscape dynamics will lengthen this time – let's take a closer look

Source: Mezzopointe, LLC customized analysis: 15-Year Historical Overview (2009-2024); N = 2,500 Pediatric Clinical Trials. Primary data sources: Evaluate Pharma, Trial Trove and IPD Analytic, accessed July 2024.

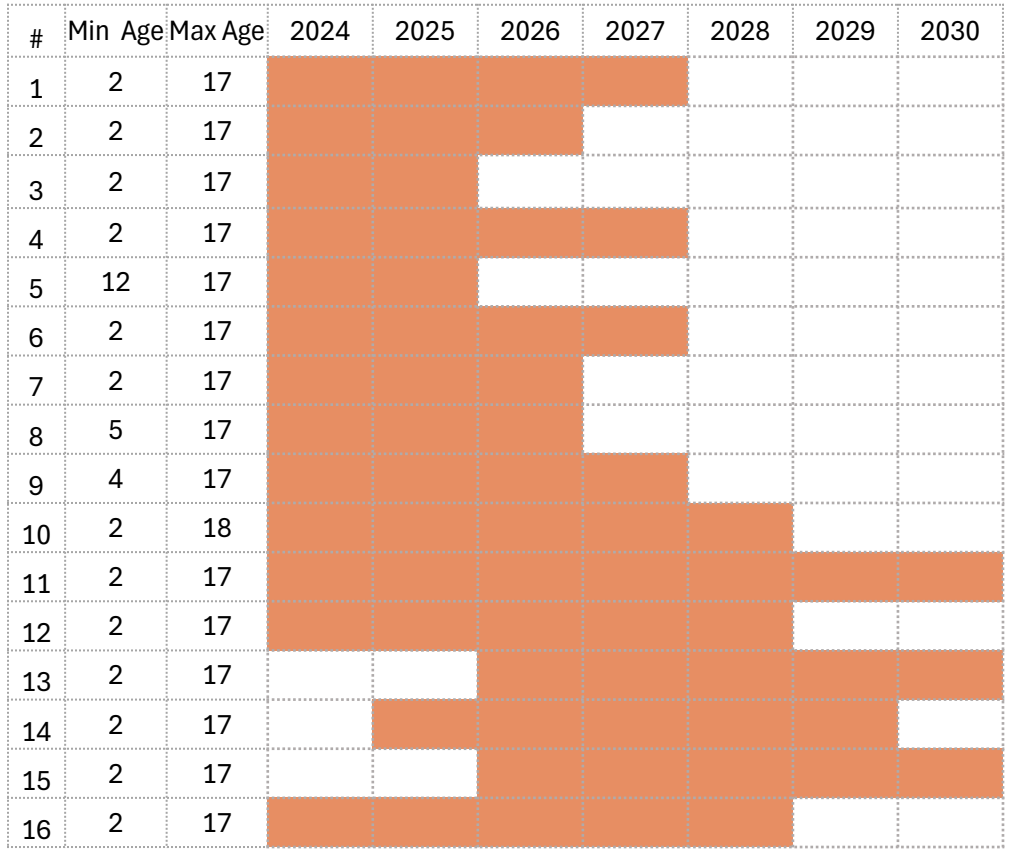
Case Study: Pediatric Ulcerative Colitis – Context

- Pediatric UC may occur at any age but is most common in adolescents [1]
- It is much more severe and aggressive in children compared to adults [1]
- There are about **2,040** children <18 years with moderate-to-severe UC in the U.S. [2]
- Based on very limited data, no differences by race in phenotypic presentation and medication usage have been noted [3]
- Differences in clinical remission were observed but they will require further exploration of SDOH [3]

1. https://www.yalemedicine.org/conditions/pediatric-ulcerative-colitis
2. AGA ABSTRACTS| VOLUME 162, ISSUE 7, SUPPLEMENT , S-643, MAY 2022, Su1589: PEDIATRIC CROHN'S AND PEDIATRIC ULCERATIVE COLITIS PRODUCT DEVELOPMENT: A PREDICTIVE LANDSCAPE VIEW Pamela L. Simpkins, Laurie Conklin, Jill Hardin, Christopher Knoll, Robert Nelson, DOI:https://doi.org/10.1016/S0016-5085(22)61511-7
3. https://doi.org/10.1016/j.jpeds.2023.113522

Case Study: Pediatric UC – Infeasibility

# of pediatric patients to enroll significantly exceeds prevalence of this disease in children due to recent surge in concurrent clinical trials. Additionally, significant off-label use in children reduces eligible pool.



#	Min Age	Max Age	2024	2025	2026	2027	2028	2029	2030
1	2	17							
2	2	17							
3	2	17							
4	2	17							
5	12	17							
6	2	17							
7	2	17							
8	5	17							
9	4	17							
10	2	18							
11	2	17							
12	2	17							
13	2	17							
14	2	17							
15	2	17							
16	2	17							

2k U.S. prevalence, pediatric UC, Mod-Severe [1]

415 Children are prescribed drugs off-label , UC Mod-Severe (20%) [2]

16 Currently active or planned pediatric trials, UC Mod-Severe

20 Years to complete the current trials [1]

1. AGA ABSTRACTS| VOLUME 162, ISSUE 7, SUPPLEMENT , S-643, MAY 2022, Su1589: PEDIATRIC CROHN'S AND PEDIATRIC ULCERATIVE COLITIS PRODUCT DEVELOPMENT: A PREDICTIVE LANDSCAPE VIEW
Pamela L. Simpkins, Laurie Conklin, Jill Hardin, Christopher Knoll, Robert Nelson, DOI:https://doi.org/10.1016/S0016-5085(22)61511-7
Note: Listing of 16 pediatric trials (current or planned): Trial Trove and IPD Analytics (adult PIII pipeline), accessed July 2024
2 Source: Commercial Claims and Encounters Database, The IBM MarketScan Commercial Claims and Encounters (CCAE) Database contains data from adults and pediatrics insured by employer sponsored plans (i.e., individuals not eligible for Medicare). Use of vedolizumab only in 2023. Off-label use is likely higher when other approved drugs are considered.

Case Study: Pediatric Asthma – Context

- Leading chronic disease in children
- Prevalence: **4.5 million** children [1]
- Black children are nearly **2 times** more likely to have asthma than non-Hispanic White children [1]
- Boys are more likely to have asthma than girls (reverse is true in adults) [1]
- 3rd week in September is **"Asthma Peak Week"** (after school starts) [2]
- Top 20 cities with worse outcomes are called "**Asthma Capitals**" [2]

1. Asthma Facts.
2. Asthma Capitals Report 2023

Case Study: Pediatric Asthma – Strategies

Diversity > Goal

Asthma Example	Total # Years
Blinded Study – goal	3.0
Asthma Median	6.5

Source: Anecdote based on interview with a blinded industry sponsor; permission granted.

▲ = Top 20 Asthma Capitals (highest asthma prevalence, ER visits and deaths) Asthma Capitals Report 2023

Target Asthma Capitals:

Highest asthma prevalence, ER visits and deaths

Go to where patients are…

- ✓ Prevalence
- ✓ "Asthma Capital" concentration
- ✓ Diverse catchment areas

Patient-centered strategy…

- ✓ Community programming
- ✓ Adolescents in adult trials
- ✓ Extrapolation from adult data

Observations that are Unique to Pediatrics

Positive Impact on Quality, Speed and Efficiency

- Adolescents in adult trials, when appropriate
- Extrapolation – borrowing of data from adults or older cohorts of children
- Site selection coupled with family engagement at community level
- Study designs – open label, child-friendly schedule, etc.

Enrollment Challenges

- Small populations dispersed across the world
- Multiple products enrolling concurrently in small populations
- Complex SDOH
- Off-label use due to gap: adult labeling vs. pediatric label changes

Historical Analysis
Key Takeaways

- Pediatric product development continues to be long and complex
- End-to-end time to completion and efficiency remained stable
- History provides important context needed to build effective strategies, including those needed to achieve appropriate representation
- Tailored approaches should emphasize quality, speed and efficiency

The historical baseline metrics presented herein will be useful in measuring progress in the future

Pediatric Product Development

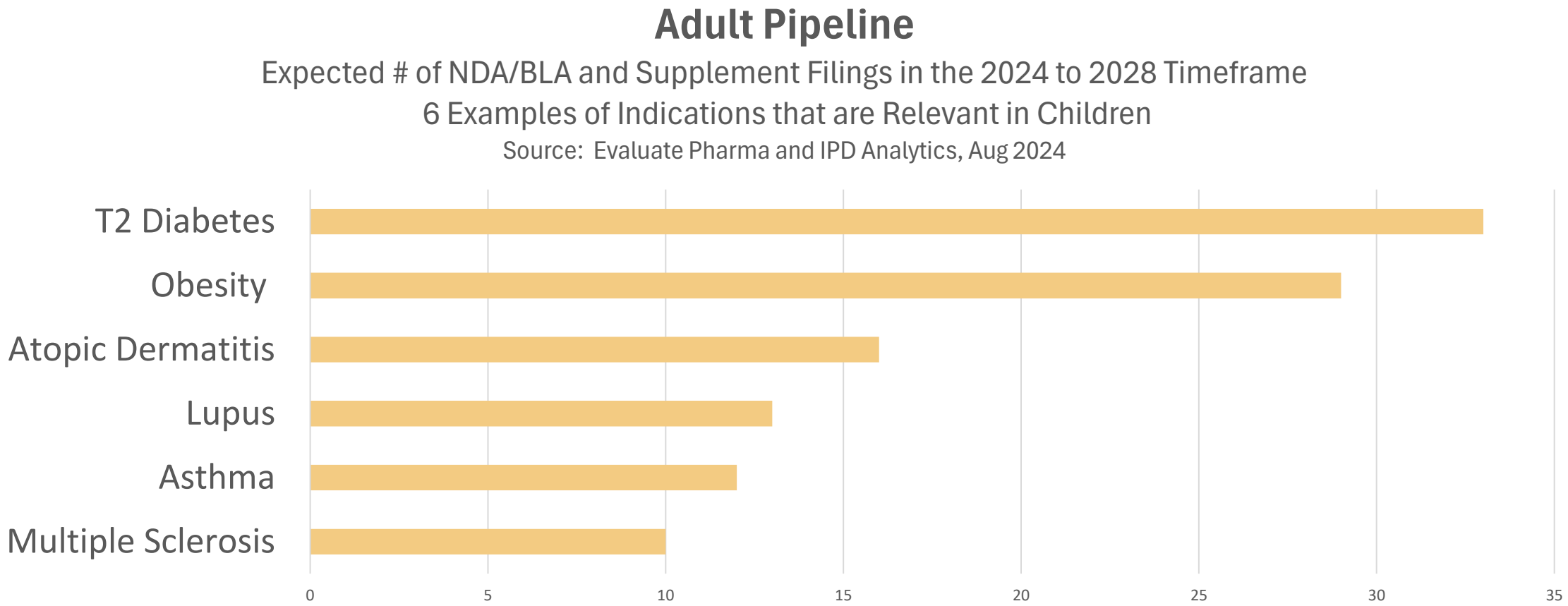
1. Historical characterization of industry-sponsored pediatric clinical trials
2. **Prospective view of upcoming industry-sponsored pediatric clinical trials**

Prospective View of Pediatric Clinical Trials

Since **67%** [1] of pediatric clinical trials are required under PREA [2] and, therefore, typically follow adult product approvals, the adult pipeline is often used to provide a directional feel for upcoming industry-sponsored pediatric clinical trial activity.

1. Source: Mezzopointe, LLC customized analysis: 15-Year Historical Overview (2009-2024); N = 2,500 Pediatric Clinical Trials. Primary data sources: Evaluate Pharma, Trial Trove and IPD Analytics, accessed July 2024.
2. PREA is the Pediatric Research Equity Act. PREA gives FDA the authority to require pediatric studies in certain drugs and biological products. Studies must use appropriate formulations for each age group. The goal of the studies is to obtain pediatric labeling for the product.

Current Adult Pipeline



What insights from the historical landscape can we apply to these future pediatric trials?

Caveat: Pipeline failures, attrition & other factors may significantly alter this picture. It is not a prediction of pediatric trials, it only provides a rough idea for directional plans.

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Excludes oncology since MOA (not indication) must be evaluated for relevance in children's cancers pursuant to FDARA 504.

Prospective View
Key Takeaways & Questions

- Significant upcoming pediatric trial activity in 10+ indications relevant to pediatrics (only 6 were highlighted here)
- What insights were gleaned from the historical analysis that can be applied to the upcoming pipeline of industry-sponsored pediatric clinical trials?
- How do we achieve the diversity that reflects the population intended for treatment?

Work We Can Do Together

- Strategies for improving diversity in clinical trials will benefit from the historical and prospective information shared in this presentation
- Let's use this information to build our knowledge and formulate actionable strategies that benefit all children so that they have speedy access to the therapies they need

Thank you

Q&A

Thank You

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