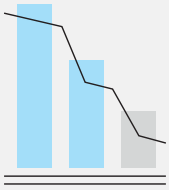
# PEDIATRIC DRUG DEVELOPMENT ISSUE BRIEF:
## Progress in a Critical but Challenging Space

**Researching and developing innovative and therapeutically appropriate medicines for children is an important priority for America's biopharmaceutical research companies. Developing medicines for children requires specific, tailored approaches to clinical trial recruitment and conduct, study design, and assessing outcomes. By design, this work is complex, iterative in nature and builds on prior scientific advances.**

**While significant progress has been made over the past few decades, unmet medical needs remain, particularly in scientifically challenging disease areas. The policy frameworks that protect incentives for research and development and account for the nuances of developing medicines for children are essential for spurring continued progress.**

### TAILORED APPROACHES ARE NEEDED TO DEVELOP INNOVATIVE MEDICINES FOR CHILDREN

Research in children is conducted only after taking **special ethical and medical considerations** into account.



**Small patient populations make it challenging** to recruit for and enroll patients in clinical trials.

Diseases in children are often biologically different than those in adults, requiring **additional assessments of medicine safety and efficacy**.

**Children respond differently to medicines than adults**, requiring unique dosage and formulation considerations.

### Key Laws Fostering Pediatric Drug Development

To address the unique considerations and challenges of developing drugs and biologics for children and help ensure that pediatric-specific information is appropriately available, Congress originally enacted pediatric drug development incentives in 1997. These provisions were reauthorized throughout the 2000's and ultimately permanently authorized by the Pediatric Research Equity Act (PREA) and the Best Pharmaceuticals for Children Act (BPCA) in 2012. These policies work together to foster pediatric drug development, enabling biopharmaceutical companies to continue making significant investments in critical research areas for children, such as chronic and rare diseases.

**Pediatric Research Equity Act (PREA):** Authorizes FDA to require pediatric research for certain indications for which the sponsor is seeking approval in adults and product formulations appropriate for children.

**Best Pharmaceuticals for Children Act (BPCA):** Complements PREA and provides incentives (six months of added exclusivity) to encourage manufactures to conduct pediatric studies of medicines with the potential for use in children.

## BY THE NUMBERS

**20+ Years of Pediatric Innovation**
PREA and BPCA have resulted in significant increases in pediatric research, product approvals, and expanded labeling for pediatric populations:

**770+ pediatric studies completed**
since the first temporary reauthorization of BPCA and PREA in 2007,[1] with 323,000+ children participating

**800+ labeling updates**
reflecting pediatric information made since 2007[1]

**Over 160 approved medicines**
granted pediatric exclusivity under BPCA since 2007[2]

**2,630+ industry-sponsored pediatric clinical trials**
underway worldwide[3]

**Progress in Pediatric Health Outcomes**
Advancements in treatment have led to improvements in health outcomes for children:

A child born today can expect to live
**27 YEARS LONGER**
than a child born a century ago[4]


Since 1980, the mortality rate from all types of cancer among children and teens has dropped by
**MORE THAN 50%**[5]


Since 2005, the U.S. infant mortality rate
**DECLINED 21%**[6]


## Advancing Innovative Treatment Options for Children

Supported by the BPCA and PREA policy framework, researchers have made strong progress in advancing clinical research and treatment options for children. Pediatric drug development relies on the continued research and development of medicines, many times first approved for use in adults, where scientists and physicians continue to generate information to develop medicines for new indications. Treatment advances in pediatric populations are a profound reminder that innovation does not stop once a medicine is approved. The future of treatments for America's children depends on this.

However, the recent passage of the Inflation Reduction Act (IRA) puts this progress at risk. The IRA imposes price setting for certain medicines after only nine years of U.S. Food and Drug Administration (FDA) approval, far earlier than the average time of 13-14 years that companies currently have until they face generic competition for marketed products. Companies are being forced to weigh the costs and high risk associated with developing new medicines and pursuing post-approval research against the time they have to achieve a return on investment. The IRA's drug price setting provisions are undermining long-standing incentives for innovation across a range of areas, including pediatric research. Indeed, the IRA's compressed timelines, fail to account for the additional incentive provided by pediatric exclusivity, directly undermining the provisions of BPCA that have proven so successful.

## Looking Ahead

The current legal framework of BPCA and PREA carefully balances both incentives and requirements for pediatric research, fostering a research ecosystem to drive drug development for children forward. Continued investment in research that reflects the unique needs of pediatric patients is key to improving the health of children with a range of diseases, including cancers, genetic diseases, and autoimmune conditions. Health care stakeholders and policymakers must work together to preserve current regulatory frameworks and incentives that spur a thriving research ecosystem.

# Case Studies in Pediatric Drug Development

## HIV-1: New Method of Administration Transforming Treatment and Improving Adherence for Adolescents

HIV is a disease impacting both adolescents and adults. The U.S. Centers for Disease Control and Prevention reported that in 2018 people 13-24 years old account for 21% of all new HIV diagnoses in the U.S.[7] Adherence for this population can be a challenge for a variety of reasons, which is why having multiple treatment options, including a simple, long-acting injectable regimen, is important.

A medicine (cabotegravir; rilpivirine) first approved in January of 2021 as a once monthly injection for adults living with HIV-1, was approved in February 2022 to be administered every 2 months in adults with HIV-1. Then in March 2022 the medicine was approved for use in adolescents who are 12 and older. This is the first and only complete long-acting HIV-1 treatment regimen and the first to be made available to eligible adolescents.[8] The study of the long acting injectable also enrolled caregivers of the adolescents with HIV to take part in an interview to contribute to the evaluation of the tolerability and acceptability of the therapy, resulting in favorable feedback overall.[9]

## Chronic Graft-Versus-Host Disease: Continued Research Results in First Approved Treatment for Kids

Chronic graft-versus-host disease (cGVHD) is a rare condition that can occur in patients after receiving a blood or bone marrow transplant, often related to blood cancer treatment. About 35% of the estimated 8,000 patients who undergo a life-saving stem cell transplant per year develop cGVHD which requires treatment. cGVHD is also the most common cause of death after a transplant with healthy cells from a donor.

In 2017, ibrutinib became the first treatment approved in the U.S. for adult patients with cGVHD who have tried and failed on at least one previous medicine. In August of 2022, the FDA approved the use of this medicine for the treatment of pediatric patients one year and older with cGVHD who have tried and failed on one previous medicine. This is the first approved treatment option for children under 12 and the only drug class of its kind (Brutons tyrosine kinase inhibitor or BTKi) for a pediatric population.[10] This approval gives health care professionals another effective treatment option for both pediatric and adult patients. This approval also includes a specific oral formulation designed for children, providing a helpful alternative.[10]

## Juvenile Idiopathic Arthritis: Advancing the Treatment Paradigm for a Group of Rare Pediatric Diseases

Though juvenile idiopathic arthritis (JIA) was formerly referred to as "juvenile rheumatoid arthritis," it is not a pediatric version of an adult disease. Rheumatoid arthritis (RA) is a chronic disease that primarily impacts adults throughout their lifetime. Unlike RA, children often outgrow JIA—a collection of six rare inflammatory conditions—but the disease can significantly affect bone development in a growing child.[11] Given the unique pathology of the pediatric condition, it is critical that therapeutic approaches for treating adults with this disease are evaluated specifically in children to ensure safety and efficacy.

Over the past decade, post-approval research and development of existing medicines approved for use in adults has provided children with many forms of JIA the ability to moderate and slow the progression of these diseases and prevent significant disability later in life. For adults with RA, the first Janus kinase inhibitor (JAK), was approved in 2012. Subsequent research led to the approval of this medicine for patients two years and older who have a particular form of JIA impacting the joints (polyarticular JIA).[12] As an oral formulation, the medicine provided a critical treatment option for these pediatric patients. Similarly, in 2020 a type of medicine referred to as a tumor necrosis factor (TNF) inhibitor, originally approved for adults with RA, received two additional approvals: one for polyarticular RA and another for children and adolescents with psoriatic arthritis, another form of JIA. Prior to this approval, children with psoriatic arthritis did not have any disease-modifying treatment options.[13]

## Pediatric Cancer: Expanding Treatment Options and Survival in Pediatric Leukemias

Continued research of existing treatments is particularly important in cancer, where existing cancer treatments can be used across a range of cancer types as researchers learn more about the underlying diseases. This is particularly important in bringing new treatments to children living with cancer. For example, a novel immunotherapy, blinatumomab, was originally granted accelerated approval in December 2014 for the treatment of a specific form of advanced B-Cell Acute Lymphoblastic Leukemia (ALL) in adults.[14] This medicine harnesses the patient's own immune cells to target and attack cancer cells. In 2016, after extensive research into the application of this immunotherapy in children, blinatumomab received a supplemental approval for the treatment of pediatric patients with the same type of ALL.[15] Most recently, in 2021, research demonstrated that the medicine significantly improved survival for children with relapsed B-cell ALL–an aggressive cancer where patients produce too many immature white blood cells.[16] The published research study outcomes showed that blinatumomab was not only more effective than chemotherapy, the previous standard of care, but also much less toxic–an impactful advance for pediatric leukemia patients.[16]

In addition, blinatumomab has been studied in and approved for use in other forms of B-Cell ALL in pediatric patients with certain minimal residual disease levels.[14] As leukemias are the most common type of cancer affecting children under the age of 14, it's also an area where we've seen a lot of progress. Continued development of treatment options for the many forms of this type of cancer is critical to continuing to improve outcomes for children living with this disease.[17]


1 Food and Drug Administration (FDA). Pediatric Labeling Changes. https://www.fda.gov/science-research/pediatrics/pediatric-labeling-changes. Updated February 10, 2023. Accessed April 5, 2023.

2 Food and Drug Administration (FDA). Pediatric Exclusivity Granted. https://www.fda.gov/drugs/development-resources/pediatric-exclusivity-granted. Updated March 2, 2023. Accessed April 5, 2023.

3 Clinicaltrials.gov with search terms "recruiting, not yet recruiting; active, not recruiting - interventional studies - child - industry." Accessed April 5, 2023.

4 National Center for Health Statistics (NCHS). National Vital Statistics Reports, Vol. 68, No. 4, United States Life Tables, 2016, Table 19. May 7, 2019. https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_04-508.pdf. Accessed April 5, 2023.

5 National Cancer Institute (NCI). Seeing a Promising Future for Progress Against Childhood Cancer. September 16, 2021. https://www.cancer.gov/news-events/cancer-currents-blog/2021/childhood-cancer-accelerating-progress-sharpless. Accessed April 5, 2023.

6 National Center for Health Statistics (NCHS). National Vital Statistics Reports, Vol. 71, No 5, Infant Mortality in the United States, 2020. September 29, 2022. https://www.cdc.gov/nchs/data/nvsr/nvsr71/nvsr71-05.pdf. Accessed April 5, 2023.

7 National Institutes of Health (NIG). HIV and Children and Adolescents. https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-and-children-and-adolescents. Updated August 19, 2021. Accessed April 5, 2023.

8 Johnson & Johnson. U.S. FDA Approves CABENUVA (cabotegravir and rilpivirine) for Adolescents, Expanding the Indication of the First and Only Complete Long-Acting Injectable HIV Regimen. March 29, 2022. https://www.jnj.com/u-s-fda-approves-cabenuva-cabotegravir-and-rilpivirine-for-adolescents-expanding-the-indication-of-the-first-and-only-complete-long-acting-injectable-hiv-regimen. Accessed April 5, 2023.

9 Lowenthal E, Chapman, J, Calabrese, K, et al. Adolescent and Parent Experiences with Long-Acting Injectables in the MOCHA Study. Presented at CROI 2022, February 12-16, 2022. https://medinfo.gsk.com/5f95dbd7-245e-4e65-9f36-1a99e28e5bba/fea1e4d7-e777-40f7-8ab7-ebc88ffd63c3/fea1e4d7-e777-40f7-8ab7-ebc88ffd63c3_viewable_rendition__v.pdf. Accessed April 5, 2023.

10 AbbVie. Children with Chronic Graft Versus Host Disease (cGVHD) May Now Be Prescribed IMBRUVICA® (ibrutinib). August 24, 2022. https://news.abbvie.com/news/press-releases/children-with-chronic-graft-versus-host-disease-cgvhd-may-now-be-prescribed-imbruvica-ibrutinib.htm. Accessed April 5, 2023.

11 Johns Hopkins Medicine. Juvenile Rheumatoid Arthritis. https://www.hopkinsmedicine.org/health/conditions-and-diseases/arthritis/juvenile-idiopathic-arthritis. Accessed April 5, 2023.

12 Food and Drug Administration (FDA). FDA Approvals in 2020 represent many firsts for children. 2020. https://www.fda.gov/media/145481/download. Accessed April 5, 2023.

13 PhRMA. A Decade of Innovation in Rare Diseases, 2012-2021. 2022. https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRMA_RD_Report_R9_Final_Updated-2-28-22.pdf. Accessed April 5, 2023.

14 Food and Drug Administration (FDA). BLINCYTO® (blinatumomab) Prescribing Information. February 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125557s021lbl.pdf. Accessed April 5, 2023.

15 Amgen. FDA Approves BLINCYTO® (blinatumomab) For Use In Pediatric Patients With Philadelphia Chromosome-Negative Relapsed Or Refractory B-cell Precursor Acute Lymphoblastic Leukemia. September 1, 2016. https://www.amgen.com/newsroom/press-releases/2016/09/fda-approves-blincyto-blinatumomab-for-use-in-pediatric-patients-with-philadelphia-chromosomenegative-relapsed-or-refractory-bcell-precursor-acute-lymphoblastic-leukemia. Accessed April 5, 2023.

16 National Cancer Institute (NCI). Blinatumomab Improves Survival in Children with Relapsed Leukemia. April 1, 2021. https://www.cancer.gov/news-events/cancer-currents-blog/2021/blinatumomab-relapsed-b-cell-leukemia-children-young-adults. Accessed April 5, 2023.

17 National Cancer Institute (NCI). Cancer in Children and Adolescents. https://www.cancer.gov/types/childhood-cancers/child-adolescent-cancers-fact-sheet. Updated November 4, 2021. Accessed April 5, 2023.