September 17, 2024

The Honorable Ron Wyden
Chairman
United States Senate Committee on Finance
221 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Mike Crapo
Ranking Member
United States Senate Committee on Finance
239 Dirksen Senate Office Building
Washington, DC 20510

Dear Chair Wyden and Ranking Member Crapo,

On behalf of the more than 30 million Americans living with one of the over 10,000 known rare diseases, the National Organization for Rare Disorders (NORD) and the EveryLife Foundation for Rare Diseases thanks the Senate Finance Committee for holding a hearing entitled "Lower Health Care Costs for Americans: Understanding the Benefits of the Inflation Reduction Act."

Our two organizations believe the Inflation Reduction Act (IRA) has the potential to have a profound impact on the rare disease community we so proudly represent, including some potential unintended negative consequences. As Congress considers further action to strengthen our health care system, we urge you to address two technical changes to the Inflation Reduction Act that will preserve the hope of the 95% of rare disease communities without disease-specific FDA approved treatment options.[1]

NORD is a unique federation of non-profit and health organizations dedicated to improving the health and well-being of people with rare diseases by driving advances in care, research, and policy. NORD was founded over 40 years ago, after the passage of the Orphan Drug Act (ODA), to formalize the coalition of patient advocacy groups that were instrumental in passing this landmark law. Since that time, NORD has been advancing rare disease research and funding to support the development of effective treatments and cures; raising awareness and addressing key knowledge gaps; and advocating for policies that support the availability of affordable, comprehensive health care, including access to safe and effective therapies.

The EveryLife Foundation for Rare Diseases is a 503(c)(3) nonprofit, nonpartisan organization dedicated to empowering the rare disease patient community to advocate for impactful, science-driven legislation and policy that advances the equitable development of access to lifesaving diagnoses, treatments, and cures. EveryLife Foundation's policy priorities are guided by the Community Congress, a diverse coalition comprised of patient advocacy organizations, biopharmaceutical industry leaders, coalition groups, and other relevant stakeholders that inform our policy efforts and provide counsel and insight on important issues impacting the rare disease community.

[1] Fermaglich LJ, Miller KL. A comprehensive study of the rare diseases and conditions targeted by orphan drug designations and approvals over the forty years of the Orphan Drug Act. 2023;18(1). doi.org/10.1186/s13023-023-02790

Our organizations are supportive of key IRA provisions, such as the $2,000 out-of-pocket spending cap and the ability to spread out monthly out-of-pocket costs for Medicare Part D starting in 2025. These aspects of the IRA ensure that more rare disease patients with Medicare coverage will be able to afford the life-altering therapies they need.

However, we recognize that most rare disease patients are still in need of new and better therapies to treat the devastating effects of their disease. Since the passage of the Orphan Drug Act, Congressional leaders and Administrations have worked to encourage further research and development into rare disease treatments. Continuing in this spirit, the IRA includes a narrow exclusion for some rare disease therapies. Unfortunately, the exclusion, as written, threatens to inadvertently disincentivize rare disease research. Thus, putting at risk the progress made from the last four decades of orphan drug incentives.

In a December 1, 2023, letter (included in Addendum A), which was joined by 170 patient organizations, we urged you to consider two technical corrections to the IRA's orphan drug exclusion to ensure appropriate continued incentives to invest in the research and development necessary to address the vast unmet medical need of the rare disease community. Our asks were to:

1. **Clarify that the number of orphan designations FDA grants a product has no effect on its eligibility for the IRA's orphan drug exclusion; and**
2. **Maintain the purpose of the orphan drug exclusion by clarifying an orphan product becomes negotiation eligible 7 or 11 years after it loses that exclusion.**

To continue the efforts to develop safe and effective therapies to treat the millions of Americans living with rare diseases, we encourage you to support these two, small, technical corrections. Further information can be found in our prior letter in Addendum A below. Additionally, in Addendum B, we have included a more detailed explanation of the proposed technical corrections.

Thank you for your consideration. For more information, please contact:

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Addendum A:

The 170 undersigned organizations representing patients, families, and the rare disease community thank you for your continued commitment to policies promoting the health and well-being of the more than 30 million Americans living with a rare disease. As Congress considers further action to strengthen our health care system, we urge you to address two technical changes to the Inflation Reduction Act that will help preserve the hope of the 95% of rare disease communities without disease-specific FDA approved treatment options[1], yet will not change the number of approved indications a product can have before becoming eligible for Medicare negotiation.

The Inflation Reduction Act of 2022 (IRA) enabled the Centers for Medicare & Medicaid Services (CMS) to negotiate the price of some prescription drugs. For too many Americans living with rare diseases, out- of-pocket prescription drug costs create significant financial barriers to access. Our organizations strongly support key IRA provisions such as the $2,000 out-of-pocket spending cap and the ability to spread out monthly out-of-pocket costs for Medicare Part D starting in 2025. These aspects of the IRA will ensure that more rare disease patients with Medicare coverage will be able to afford the life-altering therapies they need.

However, our optimism is balanced with the reality that most rare disease patients are still in urgent need of new and better therapies to treat the devastating effects of their rare disease. Over the last 40 years, starting with the passage of the Orphan Drug Act, Congressional leaders and Administrations have consistently worked to encourage more research and development into rare disease treatments. In continuing to recognize the unique needs of the rare disease community, the IRA's Medicare Drug Price Negotiation Program (MDPNP) includes a narrow exclusion for some rare disease therapies. Unfortunately, confusing legislative language inadvertently disincentives rare disease research, putting the progress yielding from the orphan drug incentives that so effectively spurred rare disease drug development over the last four decades at risk.

Specifically, our organizations urge you to consider the following two technical fixes to the IRA's orphan drug exclusion to ensure appropriate continued incentives to invest in the research and development necessary to address the vast unmet medical need of the rare disease community:

1. ***Clarify that the number of orphan designations FDA grants a product has no effect on its eligibility for the IRA's orphan drug exclusion.***

Under current law, orphan drugs with only one orphan designation AND one approved indication (or multiple approved indications all tied to the same rare disease designation) are excluded from MDPNP eligibility. However, as soon as the drug is designated for a second disease, even without any associated FDA approved indications, it will lose its negotiation exclusion.

The current IRA statute fails to recognize the critical difference between designations, which only unlock R&D incentives, and approved indications, which allow for an orphan drug to enter the market. Orphan drug designations typically happen early in the clinical research process, based on data from animal models or very early clinical studies; the purpose is to unlock R&D

incentives established by the ODA, NOT to obtain FDA's approval to market a drug. FDA approval for a specific indication occurs much later, after the product has been extensively studied in clinical trials and shown to be safe and effective for that specific condition and/or patient population. Many drugs fail in the R&D stage and granting a product an orphan drug designation does NOT mean a drug will ultimately be approved to treat the associated orphan indication. In fact, to date, there have been more than 6600 orphan designations made by the FDA, but only approximately 1160 FDA approved indications for orphan products.[2]

Congress, clarify that the number of orphan designations granted to a product has no effect on its eligibility for the IRA's orphan drug exclusion; this will help encourage much-needed continued research and development into rare diseases, most of which do not have any FDA approved therapies.

2. ***Maintain the purpose of the orphan drug exclusion by clarifying an orphan product becomes negotiation-eligible 7 or 11 years after it loses that exclusion.***

To account for the need of drug sponsors to recoup R&D costs, products that otherwise meet the criteria for the MDPNP are not negotiated until they have been on the market for 7 or 11 years - for small molecule drugs or biologics, respectively. Yet, under current law, a similar time is not granted for orphan drugs that lose eligibility for the orphan drug exclusion. Once the orphan drug loses its eligibility, it is immediately negotiation eligible seven or eleven years after the product's very first approval, as if the exclusion never happened. This is true even if the orphan drug loses eligibility for the exclusion many years after the first approval. In fact, a recent article published in JAMA found that on average it takes 4.5 years for a novel orphan drug to obtain a second approved indication.[3] This significantly magnifies existing disincentives to further develop an orphan drug to treat additional rare diseases.

Congress, clarify that a previously excluded product will become negotiation eligible 7 to 11 years after losing eligibility for the orphan drug exemption (rather than from the very first approval); otherwise, manufacturers will have essentially no incentive to pursue continued research and clinical trials to treat additional rare diseases.

To continue long-standing efforts to develop safe and effective therapies to treat the millions of Americans living with rare diseases, our patient organizations urge Congress to support these two technical corrections to the IRA. The proposed changes do not fundamentally alter the intent of the IRA's orphan drug exclusion, but instead serve to reinforce the decades long commitment Congress has made to ensuring everyone has an opportunity for a safe and effective therapy, regardless of the rarity of their condition.

Sincerely,

EveryLife Foundation for Rare Diseases
National Organization for Rare Disorders

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[2] FDA Orphan Drug Designations and Approvals Database. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/
[3] JAMA Network Open. 2023;6(8):e2329006. doi:10.1001/jamanetworkopen.2023.29006 (Re

ALS Association
American Cancer Society Cancer Action Network
Friedreich's Ataxia Research Alliance
Leukemia & Lymphoma Society
National Health Council
A Twist of Fate-ATS
ACTA2 Alliance
Abetalipoproteinemia & Related Disorders Foundation
Adenoid Cystic Carcinoma Research Foundation
Adrenal Insufficiency United
African Americans with Ataxia Association
Alliance for Aging Research
Alport Syndrome Foundation
Alström Syndrome International
American Kidney Fund
American Medical Women's Association
Amyloidosis Research Consortium
Angelman Syndrome Foundation
APS Foundation of America, Inc
Arthritis Foundation
Asbestos Disease Awareness Organization (ADAO)
Association for Creatine Deficiencies
Association for the Bladder Exstrophy Community Autoimmune Association
Avery's Hope
BDSRA Foundation
CACNA1A Foundation
CancerCare
CDH International
Center for Patient Advocacy Leaders (CPALs)
Centre for Community-Driven Research Chondrosarcoma CS Foundation, Inc.
Choroideremia Research Foundation
Chronic Disease Coalition
Coalition to Cure Calpain 3
Congenital Hyperinsulinism International
COPD Foundation
CSNK2A1 Foundation
Cure 4 The Kids Foundation Cure CMD
Cure GM1 Foundation Cure HHT
Cure Mito Foundation Cure MLD
Cure Sanfilippo Foundation
Cure VCP Disease, Inc
CURED Nfp
DADA2 Foundation
Danny's Dose Alliance
Dravet Syndrome Foundation
EB Research Partnership

Epilepsy Foundation
Fabry Support & Information Group
FACES: The National Craniofacial Association
Family Heart Foundation
Foundation for Angelman Syndrome Therapeutics (FAST)
Foundation to Fight H-ABC
Foundation for Sarcoidosis Research
Galactosemia Foundation
GBS|CIDP Foundation International
Global Genes
GRIN2B Foundation HCU Network America
Hepatitis B Foundation
Hermansky-Pudlak Syndrome Network Inc.
Hide & Seek Foundation
Histiocytosis Association, Inc.
Hope For Danté
Huntington's Disease Society of America
Hydrocephalus Association
Hypertrophic Olivary Degeneration Association
ICAN, International Cancer Advocacy Network
IDefine
IgA Nephropathy Foundation
Immune Deficiency Foundation
Indo US Organization for Rare Diseases (IndoUSrare)
International Foundation for CDKL5 Research
International Pemphigus & Pemphigoid Foundation
International Waldenstrom's Macroglobulinemia Foundation (IWMF)
Jack McGovern Coats' Disease Foundation
Jamal's Helping Hands
Juju and Friends CLN2 Warrior Foundation
Ketotic Hypoglycemia International
KrabbeConnect
Krishnan Family Foundation
Let's Cure ACC
Leukodystrophy Newborn Screening Action Network
Li Fraumeni Syndrome Association
Little Hercules Foundation
Lupus and Allied Diseases Association, Inc.
Mackenzie’s Mission
Muscular Dystrophy Association
MdDS Foundation
Mission: Cure
Mississippi Metabolics Foundation
MitoAction
MLD Foundation
Musella Foundation For Brain Tumor Research & Information, Inc

Myasthenia Gravis Association
Myasthenia Gravis Foundation of America (MGFA)
Myocarditis Foundation
Myositis Support and Understanding NAIT babies
Narcolepsy Network
National Ataxia Foundation
National Eosinophilia Myalgia Syndrome Network
National Fragile X Foundation
National MALS Foundation
National MPS Society
National Perinatal Association
National PKU Alliance
National Psoriasis Foundation
NephCure
NTM Info & Research
Northwest Parkinson's Foundation
Organic Acidemia Association Corporation
Parent Project Muscular Dystrophy
Partnership to Fight Chronic Disease
Patient Empowerment Network
Petronille Healthy Society
PF Warriors
Phelan-McDermid Syndrome Foundation
Pompe Alliance
Project Alive
Propionic Acidemia Foundation
Pulmonary Hypertension Association
PWSA | USA
Rare And Black
RareKC
Rare New England
Rubix LS
Sarcoidosis of Long Island
SCA27b Ataxia Foundation
SCAD Alliance
Sick Cells
Sickle Cell Disease Association of America
Sickle Cell Association of Kentuckiana
Spastic Paraplegia Foundation, Inc.
Super T's Mast Cell Foundation
SYNGAP1 Foundation
T.E.A.M. 4 Travis
Team Telomere
Team Titin, Inc.
Texas Rare Alliance
The Akari Foundation

The Bluefield Project to Cure Frontotemporal Dementia
The Bonnell Foundation: Living with cystic fibrosis
The Desmoid Tumor Research Foundation
The E.WE Foundation
The Fairy Goddess Mother Project
The Foundation for Casey's Cure, Inc.
The Global Foundation for Peroxisomal Disorders
The LCC Foundation
The Mast Cell Disease Society
The Oxalosis and Hyperoxaluria Foundation
The RYR-1 Foundation
The Sudden Arrhythmia Death Syndromes (SADS) Foundation
Thrive with Pyruvate Kinase Deficiency Organization
Trisomy 12p Support Group
Undiagnosed Diseases Network Foundation United
MSD Foundation
Uriel E. Owens Sickle Cell Disease Association of the Midwest
Usher 1F Collaborative
Usher Syndrome Society
Vasculitis Foundation
wAIHA Warriors, Inc.
World Alliance of Pituitary Organizations
Yellow Brick Road Project

Addendum B:

Minor changes to the Inflation Reduction Act (IRA) will make a big difference for rare disease patients

For the first time, empowered by the Inflation Reduction Act of 2022 (IRA), the Centers for Medicare & Medicaid Services (CMS) will negotiate the price of some prescription drugs. The IRA included a limited exclusion for some rare disease therapies from the negotiation program, but the narrow nature of that exclusion could undermine some of the critical incentives established by the Orphan Drug Act.

Under current law, orphan drugs that have only one orphan designation AND one approved indication (or multiple approved indications all tied to the same designated rare disease) are excluded. However, as soon as the drug is designated for a second disease, even without any associated approvals, it will become negotiation eligible–and the clock for when a product could be selected for negotiation starts at the date of the drug's very first approval, even if the second designation or additional approval occurs many years later.

Two technical changes to the IRA will help preserve the hope of the 95% of rare disease communities without disease-specific FDA approved treatment options, yet will not change the number of approved indications a product can have before becoming eligible for Medicare negotiation.

CONGRESSIONAL ASK #1:

Clarify that the number of orphan designations FDA granted to a product has no effect on its eligibility for the IRA's orphan drug exclusion.

- Designations open access to incentives to conduct further clinical research to see if a product could be an effective treatment in additional populations or diseases.
- Designations do NOT allow a product to be marketed and therefore should not be tied to any policies affecting price or access of approved products.

CONGRESSIONAL ASK #2:

Maintain the purpose of the orphan drug exclusion by clarifying an orphan product becomes negotiation-eligible 7 or 11 years after it loses that exclusion.

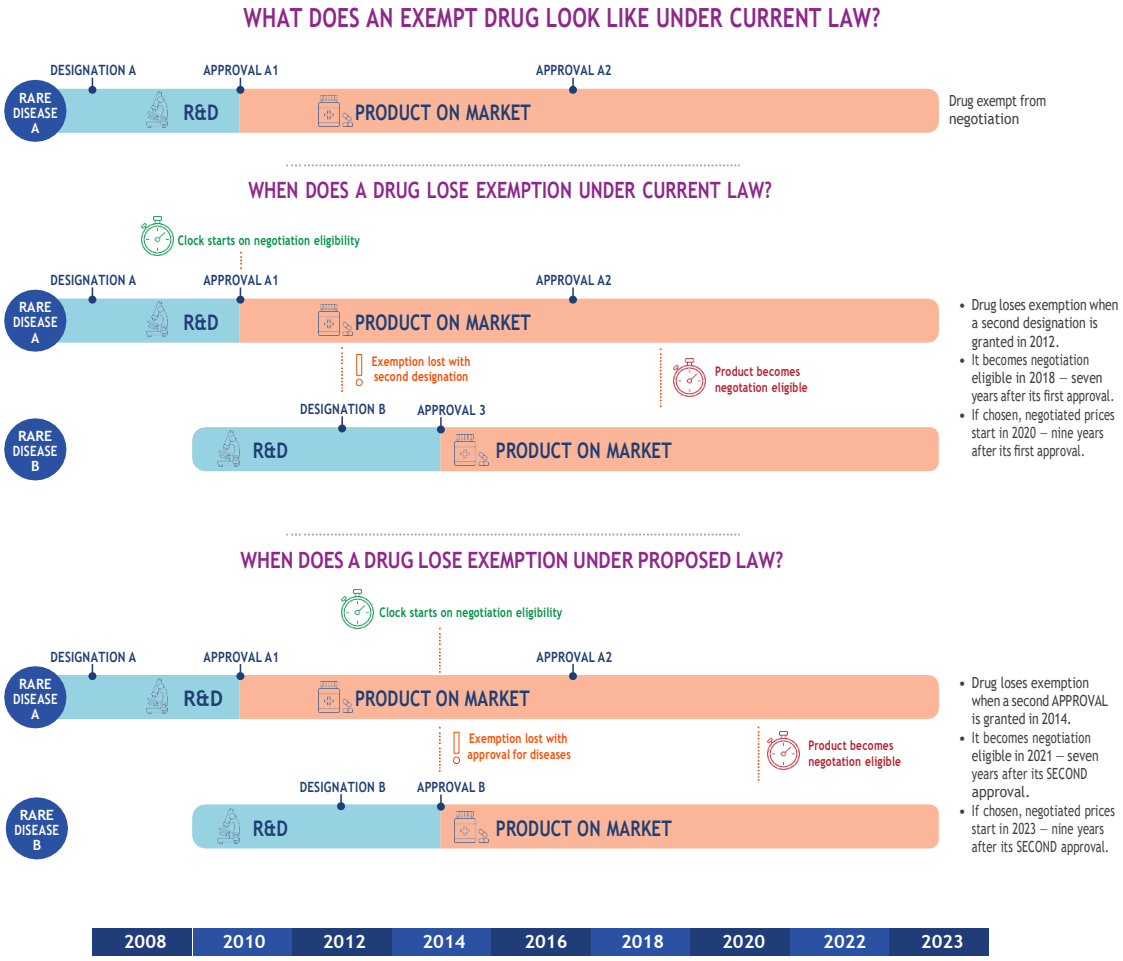
- Tying eligibility for negotiation strictly to an orphan product's first approved indication eliminates any incentive for drug companies to pursue additional rare disease indications.
- Ensuring the clock doesn't start until the exclusion is lost may encourage drug companies to continue to study a drug's potential to treat additional rare diseases.

DESIGNATIONS AND APPROVED INDICATIONS ARE NOT THE SAME

	ORPHAN DRUG DESIGNATION	FDA-APPROVED INDICATION
TIMING	**Early** in drug development	At the **end** of drug development and FDA premarket review
PURPOSE	**Unlock R&D incentives** such as: • Tax credits for qualified clinical trials • Exclusion from FDA user fees • Potential seven years of market exclusivity **if approved**	Allow for **marketing** of the drug in the US
REQUIRED EVIDENCE	The target disease affects **fewer than 200,000** Americans & there is some preclinical or early clinical evidence that the drug candidate may plausibly work for the rare disease	Through extensive clinical studies in patients with the target disease, the drug has been **shown safe and effective** for its intended purpose
NEXT STEPS IN THE PRODUCT'S LIFE CYCLE	**Study** the drug in patients with the target disease	Begin to **market** the drug in the US
EXAMPLE	*Treatment of rare disease x*	*Treatment of rare disease x in patients 12 years and older who have confirmed mutation AB*
SINCE PASSAGE OF THE ODA IN 1983	**6500+ orphan designations**	**1150+ approved indications**

The IRA's narrow orphan drug exclusion threatens continued rare disease drug development and repurposing efforts

Example: One small molecule orphan drug candidate with R&D programs for two different rare diseases



For too many Americans living with rare diseases, out-of-pocket prescription drug costs create significant financial barriers to access. However, approximately 95% of all known rare diseases lack an FDA approved treatment. **The hope of millions of Americans with unmet medical needs rests in continued research and development into new and better therapies**. Recognizing this dire need and the unique challenges that complicate rare disease drug development, a succession of Administrations and Congresses over the last 40 years have created and maintained incentives and policies to encourage more R&D into rare disease treatments.

That is why the IRA included a very narrow exclusion for some rare disease therapies from the Medicare Drug Price Negotiation Program (MDPNP). Unfortunately, that exclusion did not fully protect the orphan product incentives we've worked so hard to establish and maintain. The good news is that minor changes will make a big difference for rare disease patients.

Some aspects of the IRA will help make it more affordable for rare disease patients with Medicare to access the therapies they need. Our organizations strongly support provisions such as capping annual out-of-pocket costs and making it possible to spread out monthly costs for Medicare Part D starting in 2025.

For more information please contact:
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