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NATIONAL HEALTH COUNCIL
NORD National Organization for Rare Disorders
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The Akari Foundation
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The Mast Cell Disease Society
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RYR-I FOUNDATION
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fast
HOPE for Dante'
"Batting against Batten Disease"
Sarcoidosis OF LONG ISLAND
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We C.A.R.E.
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EB RESEARCH PARTNERSHIP
Amyloidosis Research Consortium
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Global Genes
Allies in Rare Disease
Find a Cure for HMERF
SYNGAP1 FOUNDATION
RESEARCH EDUCATION ADVOCACY
Oxalosis & Hyperoxaluria Foundation
STEPPING STONES TO A CURE
FOUNDATION TO FIGHT H-ABC
SICK CELLS
CS
ABL+ Foundation
LDNBS
HEPATITIS B FOUNDATION
Hydrocephalus Association
angelman SYNDROME FOUNDATION
MACKENZIE'S MISSION
FACES
NATIONAL CRANIOFACIAL ASSOCIATION
MYOSITIS SUPPORT & UNDERSTANDING
Alstrom Syndrome International
ASI
MISSISSIPPI MMF METABOLICS FOUNDATION
Cure MLD
USHER 1F COLLABORATIVE
Team Tilin
Pompe Alliance
THE FAIRY GODMOTHER PROJECT
iWMF International Waldenstrom's Macroglobulinemia Foundation
APS Foundation of America
MEDICAL WOMEN'S ASSOCIATION
PAF
COPD FOUNDATION
CURED Campaign Urging Research for Eosinophilic Disease
www.CuredFoundation.org
CHI Congenital Hyperinsulinism International
Prader-Willi SYNDROME ASSOCIATION | USA SAVING AND TRANSFORMING LIVES
Patient Empowerment Network
Hypertrophic Olivary Degeneration Association
GFPD GLOBAL FOUNDATION for PEROXISOMAL DISORDERS
SCAD ALLIANCE
SPONTANEOUS CORONARY ARTERY DISSECTION
ADAO Asbestos Disease Awareness Organization
Hear Asbestos. Think Prevention.
GRIN2B Foundation
NTMir Nontuberculous Mycobacteria
NTM Info & Research, Inc.
CSNK2A1 FOUNDATION
MDA Muscular Dystrophy Association
autoimmune association
Dravet Syndrome Foundation
GBS|CIDP Foundation International
LCC Foundation
Adenoid Cystic Carcinoma Research Foundation
Galactosemia Foundation
Linked for Life
NAF National Ataxia Foundation
CURE VCP DISEASE, INC.
NEMSN
CUREGM1 FOUNDATION
MUSELLA FOUNDATION FOR BRAIN TUMOR RESEARCH & INFORMATION, INC.
HCU NETWORK AMERICA
WAPO World Alliance of Pituitary Organizations
IGA NEPHROPATHY FOUNDATION
Dedicated to finding a cure.
ican international cancer advocacy network
the virtual lifeline for proactive cancer patients
myasthenia gravis association
MGA of the heartland
TX RARE
American Kidney Fund FIGHTING ON ALL FRONTS
CACNA1A FOUNDATION
Alliance FOR AGING RESEARCH
African-Americans with ATAXIA
BLUEFIELD PROJECT
Curing FTD
IFCR International Foundation for CDKL5 Research
NATIONAL MALS FOUNDATION
curehht The Cornerstone of the HHT Community
LITTLE HERCULES FOUNDATION
UDNF Undiagnosed Diseases Network Foundation
Juju and Friends CLN2 Warrior Foundation
cure CMD a cure is among us
ippf International Pemphigus & Pemphigoid Foundation
PARTNERSHIP TO FIGHT CHRONIC DISEASE
Huntington's Disease Society of America
thrive WITH PYRUVATE KINASE DEFICIENCY ORGANIZATION
CPALs CENTER FOR PATIENT ADVOCACY LEADERS By Advocates, For Advocates
IDF Immune Deficiency Foundation
Choroideremia RESEARCH FOUNDATION
CANCERcare
Organic Acidemia Association www.oaanews.org
SPF SPASTIC PARAPLEGIA FOUNDATION, INC. #ENDPainPLS HEREDITARY SPASTIC PARAPLEGIA PRIMARY LATERAL SCLEROSIS
PF WARRIORS
E.WE Foundation
National Perinatal Association Educate. Advocate. Integrate.
Neph Cure Kidney Disease
DTRF Desmoid Tumor Research Foundation
FAMILY HEART FOUNDATION
RARE AND BLACK
HPS Hermansky-Pudlak Syndrome Network, Inc.
PETRONILLE HEALTHY SOCIETY
Jack McGovern Coats' Disease Foundation
mg MYASTHENIA GRAVIS FOUNDATION OF AMERICA For a World Without Myasthenia Gravis
HIDE & SEEK FOUNDATION for lysosomal disease research
CURE SANFILIPPO FOUNDATION CURESFF.ORG
Twist of Fate
FSIG Fabry Support & Information Group
mito ACTION
ALPORT SYNDROME FOUNDATION Hope | Action | Support
Ketotic Hypoglycemia INTERNATIONAL
EPILEPSY FOUNDATION
SICKLE CELL DISEASE ASSOCIATION OF AMERICA, INC. est. 1972
abc Association for Bladder Exstrophy Community
JAMAL'S HELPING HANDS
ADRENAL INSUFFICIENCY UNITED
NPKUA national PKU alliance
SCA27b Ataxia Foundation
CURE 4 THE KIDS FOUNDATION Clinical Excellence. Compassionate Care.
SADS FOUNDATION
SUDDEN ARRHYTHMIA DEATH SYNDROMES
ACD ASSOCIATION FOR CREATINE DEFICIENCIES
nfxf NATIONAL FRAGILE X FOUNDATION
NORTHWEST PARKINSON'S FOUNDATION
FSR FOUNDATION FOR SARCOIDOSIS RESEARCH
RNE RARE NEW ENGLAND
KrabbeConnect CONNECTING PATIENTS & RESEARCH
naitbabies.org neonatal alloimmune thrombocytopenia
Trisomy 12p Parent Support
CDH International
NARCOLEPSY NETWORK
NATIONAL PSORIASIS FOUNDATION
IDEFINE Unlock the Potential
PHA Pulmonary Hypertension Association Empowered by hope
Arthritis Foundation
LUPUS and ALLIED DISEASES Association, Inc.
LI-FRAUMENI SYNDROME LFSA ASSOCIATION
VASCULITIS FOUNDATION
BDSRA foundation
LET'S CURE ACC
DANNY'S DOSE the VOICE for those with special needs all people
MdDS Foundation Dedicated to finding the cause and cure for MdDS
SUPER MAST CELL FOUNDATION
KRUNNAN FAMILY FOUNDATION
National MPS Society
ACTA2 Alliance

December 1, 2023

The Honorable Chuck Schumer
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Washington, D.C. 20510

The Honorable Mitch McConnell
Minority Leader
U.S. Senate
317 Russell Senate Office Building
Washington, DC 20510

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
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The Honorable Michael Johnson
Speaker
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The Honorable Hakeem Jeffries
Democratic Leader
U.S. House of Representatives
H-204, the Capitol
Washington, DC 20515

The Honorable Cathy McMorris Rodgers
Chair
House Committee on Energy and Commerce
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The Honorable Frank Pallone, Jr.
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House Committee on Energy and Commerce
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The Honorable Jason Smith
Chairman
House Committee on Ways and Means
1139 Longworth House Office Building
Washington, DC 20515

The Honorable Richard Neal
Ranking Member
House Committee on Ways and Means
1129 Longworth House Office Building
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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-

[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

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 made because of 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] FDA Orphan Drug Designations and Approvals Database.
https://www.accessdata.fda.gov/scripts/opdlisting/oopd/

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.

For more information, please contact:

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Sincerely,

EveryLife Foundation for Rare Diseases
National Organization for Rare Disorders
ALS Association
American Cancer Society Cancer Action Network
Friedreich's Ataxia Research Alliance
Leukemia & Lymphoma Society
National Health Council
A Twist of Fate-ATS
Abetalipoproteinemia & Related Disorders Foundation
ACTA2 Alliance

[3] JAMA Network Open. 2023;6(8):e2329006. doi:10.1001/jamanetworkopen.2023.29006 (Re

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