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BY ELECTRONIC DELIVERY

Health Policy and Analytics Medicaid Waiver Renewal Team
Attn: Michelle Hatfield
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Sent via email: 1115Waiver.Renewal@dhsosha.state.or.us

RE: Comments Regarding Oregon's Draft 1115 Medicaid Waiver Demonstration Renewal

Dear Health Policy and Analytics Medicaid Waiver Renewal Team:

Sarepta Therapeutics, a leading biopharmaceutical company in precision genetic medicine for rare diseases, appreciates the opportunity to comment on Oregon Health Authority's (OHA) draft application for renewal of the Oregon Health Plan (OHP) 1115(a) Demonstration Waiver for the July 1, 2022 – June 30, 2027 demonstration period (1115 waiver application). While we appreciate OHA's stated intent to advance health equity, Sarepta has significant concerns that OHA's 1115 waiver application would do the exact opposite if implemented and exacerbate existing inequities impacting underserved populations by placing increased burden and access challenges on patients and caregivers, leading to poorer health outcomes. It would, in fact, put OHA's strategic goal to eliminate health inequities in the state by 2030 out of reach.

Specifically, under the pretext of "Paying for Population Health" in Section 3.3, Strategy 3 of the 1115 waiver application, OHA proposes to establish a closed prescription drug formulary that allows for exclusion of drugs with "limited or inadequate evidence of clinical efficacy." This approach very plainly targets exclusion of drugs approved through the Food and Drug Administration's (FDA) accelerated approval pathway – a pathway designed to address the urgent unmet medical needs of patients with serious and often life-threatening diseases – as a means to shift resources to prevention and health-related services, and to contain costs. Unfortunately, in doing so, this approach ignores the needs of the state's most vulnerable populations – including those with largely *unpreventable* rare, genetic diseases that are fatal, progressively debilitating, and lack treatment options. By the numbers, people living with rare disease collectively represent one of the largest underserved patient communities in the world. There are over 7,000 known rare diseases, 80% with genetic causes, that affect approximately 25-30 million people in the U.S., 50% of which are children. Only 5% of known rare diseases have an approved treatment. Accelerated approval may be the only hope for some of these patients to ever have a chance at a treatment that could slow or halt progression while reducing adverse impacts on their lives and those of their caregivers.

Under OHA's Section 3.3 Strategy 3, Oregon's most vulnerable patients would stand to lose access to drugs approved through the FDA's accelerated approval pathway and some therapies may never be developed, perpetuating health inequities for patients with rare, life-threatening conditions. This clearly

will not result in the economic model Oregon is striving for in a Medicaid program that focuses on rewarding health equity and improving health among underserved populations. Our specific comments and concerns are that OHA's approach:

1. Vitiates the accelerated approval pathway—a long-standing, science-based tool established by Congress and FDA to speed availability of life-saving therapies for otherwise intractable diseases with unmet medical needs—devaluing accelerated approval products and the lives of patients who depend on them;
2. Fails to meet requirements under the federal Social Security Act (SSA) section 1115 and Oregon's obligations under the Medicaid Drug Rebate Statute (SSA section 1927); and,
3. Falls far short of meaningful cost containment given drugs approved through this pathway are not a primary driver of Medicaid spending or its growth, particularly when weighed against significant potential harm to patients.

For these reasons, we respectfully urge OHA to withdraw Section 3.3, Strategy 3 from its 1115 waiver renewal application in order to stay true to its intent to drive down health disparities. Patients suffering from difficult and tragic diseases, especially where *prevention is not an option*, deserve a chance for better health outcomes with early access to treatment based on cutting-edge science.

* * *

1. **Vitiates the accelerated approval pathway—a long-standing, science-based tool established by Congress and FDA to speed availability of life-saving therapies for otherwise intractable diseases with unmet medical needs—devaluing accelerated approval products and the lives of patients who depend on them**

OHA's waiver undermines the accelerated approval pathway's purpose in providing timely patient access to safe and effective treatments for patients with high unmet need

Thirty years ago, FDA created, and Congress subsequently codified, the accelerated approval pathway to expedite the availability of novel treatments that address urgent and unmet medical needs of patients with serious and often life-threatening diseases.¹ Under the accelerated approval pathway, FDA may approve a drug that demonstrates safety and efficacy in well-controlled clinical trials where efficacy is based on a surrogate endpoint that is reasonably likely to predict clinical benefit, rather than on a clinical outcome itself.² Post-marketing confirmatory trials are then required to verify and describe the predicted clinical benefit.³ Importantly, drugs granted accelerated approval meet the same rigorous safety and efficacy standards that all medicines must meet⁴ and therefore are not considered experimental, investigational or having met a lower evidentiary standard. The accelerated approval pathway has been used "primarily in settings in which the disease course is long and an extended period of time would be required to measure the intended clinical benefit of a drug."⁵

As FDA has noted:

[A]ccelerated approval has been used extensively in the approval of drugs to treat a variety of cancers and human immunodeficiency virus (HIV) disease where an effect on tumor growth or viral load can be assessed rapidly, but demonstrating an effect on

¹ FDA, New Drug, Antibiotic, and Biological Drug Product Regulations; Accelerated Approval, 57 Fed. Reg. 58942 (Dec. 11, 1992).

² FDA, Accelerated Approval, <https://www.fda.gov/forpatients/approvals/fast/ucm405447.htm> (last updated Sept. 15, 2014).

³ FDA, Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics. May 2014.

⁴ 21 U.S.C. § 356(e)(2).

⁵ Expedited Pathways Guidance at 15.

survival or morbidity generally requires lengthy and sometimes large trials because of the duration of the typical disease course.⁶

In these disease areas, accelerated approval has driven innovation and resulted in tremendous treatment advances over the past three decades. Recognizing the significant challenges in developing treatments for rare diseases, in 2012, Congress⁷ reinforced its overwhelming, bipartisan support for the use of the accelerated approval pathway for rare diseases through the enactment of the Food Drug Administration Safety and Innovation Act (FDASIA), with the goal of bringing treatment options to rare disease patients, 95% of whom currently do not have any.⁸

FDASIA Section 901, “enhancement of accelerated patient access to new medical treatments,” both specifies the criteria for accelerated approval (including the fact that it does not relax FDA’s approval standards to which all medicines are held) and, as described in the findings provision, reflects the urgency and importance that Congress attached to this approval pathway:

"(a) FINDINGS; SENSE OF CONGRESS.—

"(1) FINDINGS.—Congress finds as follows:

"(C) ... [T]he FDA should be encouraged to implement more broadly effective processes for the expedited development and review of innovative new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions, including those for rare diseases or conditions, using a broad range of surrogate or clinical endpoints and modern scientific tools earlier in the drug development cycle when appropriate. This may result in fewer, smaller, or shorter clinical trials for the intended patient population or targeted subpopulation without compromising or altering the high standards of the FDA for the approval of drugs.

"(D) Patients benefit from expedited access to safe and effective innovative therapies to treat unmet medical needs for serious or life-threatening diseases or conditions.

"(E) For these reasons, the [pre-FDASIA] statutory authority governing expedited approval of drugs for serious or life threatening diseases or conditions should be amended in order to enhance the authority of the FDA to consider appropriate scientific data, methods, and tools, and to expedite development and access to novel treatments for patients with a broad range of serious or life-threatening diseases or conditions.

"(2) SENSE OF CONGRESS.—It is the sense of Congress that the [FDA] should apply the accelerated approval and fast track provisions set forth in section 506 of the FDCA (21 U.S.C. 356), as amended by this section, to help expedite the development and availability to patients of treatments for serious or life-threatening diseases or conditions while maintaining safety and effectiveness standards for such treatments."

The accelerated approval pathway saves valuable time for patients who cannot afford to wait. It provides an avenue for approval before confirmation of the evidence-predicted clinical benefit which could take

⁶ Expedited Pathways Guidance at 15.

⁷ Food and Drug Administration Safety Innovations Act (FDASIA). Section 901

⁸ Kaufman, Petra, et al., “From Scientific Discovery to Treatments for Rare Diseases—A View from the National Center for Advancing Translational Sciences—Office of Rare Diseases Research,” Orphanet Journal of Rare Diseases, November 6, 2018. <https://ojrd.biomedcentral.com/articles/10.1186/s13023-018-0936-x>

many years, particularly for drugs that treat complex rare diseases with very small and heterogeneous patient populations and a long, variable disease course. Surrogate endpoints and the accelerated approval pathway are not used out of convenience, but as a necessity due to the realities of rare disease drug development.

We are deeply concerned that Section 3.3, Strategy 3 of OHA's waiver application, if implemented, could prevent Medicaid beneficiaries from accessing drugs approved through this carefully-constructed approval pathway, and could effectively turn Medicaid into a healthcare program whose beneficiaries lack access to "innovative new medicines to address unmet medical needs for serious or life-threatening diseases ... including those for rare diseases." It would, in effect, prevent our most vulnerable populations from obtaining the innovative and potentially lifesaving medicines that Congress has repeatedly worked to make available to them.

Duchenne muscular dystrophy exemplifies the necessity of the accelerated approval pathway

Duchenne muscular dystrophy is a universally fatal, rare pediatric disease caused by an absence of dystrophin—a protein vital for muscle structure, function, and preservation. Without dystrophin, patients with Duchenne experience progressive muscle deterioration and weakness, irreversibly losing the ability to walk, feed themselves, and breathe unassisted over time. Premature death typically occurs in a patient's mid-to-late twenties. An unfortunate reality is that annually – in the U.S. alone – 400 patients are lost to the disease, nearly 400 lose the ability to walk, and hundreds more lose functions they will never regain – use of their arms to feed and dress themselves, use of their hands to play video games and text friends, or the ability to breathe without ventilatory support. While this trajectory is relentless and predictable, the rate of progression from patient to patient can be quite variable complicating drug development. And while treating patients with progressive diseases earlier may delay irreversible manifestations from occurring, trials may have extensive timelines when a direct clinical benefit is required to demonstrate evidence of effectiveness, especially when the rate of progression is slow. Without accelerated approval, children with Duchenne would otherwise suffer irreparable damage waiting years for verification of clinical benefit based on a validated clinical endpoint. Today, with the accelerated approvals of EXONDYS 51 in September 2016, VYONDYS 53 in December 2019, and AMONDYS 45 in February 2021, nearly 30% of the total Duchenne population has an exon-skipping therapy available that aims to restore dystrophin production and slow disease progression in different subpopulations.

OHA's proposal mischaracterizes the FDA accelerated approval pathway, which offers unique benefits and maintains FDA's rigorous approval standards

The suggestion that drugs granted accelerated approval need "more rigorous review," and that the 21st Century Cures Act expedited drug approvals "by reducing the level of evidence required for drugs to reach the market,"⁹ are demonstrably incorrect. The waiver application states that "current rules do not allow Medicaid programs to exercise discretion about whether these drugs should be covered without being fully clinically proven." By law (21 U.S.C. § 356(e)(2)), FDA must find "substantial evidence of effectiveness" to approve any drug,¹⁰ specifically including drugs granted accelerated approval.¹¹ FDA and Congress have both made clear that neither FDASIA's accelerated approval provisions nor the 21st Century Cures Act diluted FDA's approval standards.

As FDA has explained:

⁹ Oregon 1115 Medicaid Demonstration Waiver – Draft Application for Public Comment 12/1/2021.

¹⁰ 21 U.S.C. § 355(d)(5).

¹¹ 21 U.S.C. § 356(e)(2) (the statute's accelerated approval provisions are not to be "construed to alter the standards of evidence" required for approval).

Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. For effectiveness, the standard is substantial evidence based on adequate and well controlled clinical investigations. For safety, the standard is having sufficient information to determine whether the drug is safe for use under conditions prescribed, recommended, or suggested in the proposed labeling. Under accelerated approval, FDA can rely on a particular kind of evidence, such as a drug's effect on a surrogate endpoint, as a basis of approval.¹²

FDA repeatedly made the same points in adopting the 1992 accelerated approval regulations. FDA specifically addressed whether drugs approved under this pathway meet the standards for Medicaid coverage. Responding to concerns that third-party payors could decline payment for drugs receiving accelerated approval because they have "attributes of investigational drugs," FDA disagreed and stated that:

The agency expects that, because drugs approved under the accelerated approval process meet the statutory standards for safety and effectiveness, they would be eligible for reimbursement under State Medicaid programs or other third-party plans. Drug products granted accelerated approval will not be, under the law, investigational...¹³

FDA similarly responded to concerns that the accelerated approval process was inconsistent with the substantial evidence requirement of section 505(d) of the Food, Drug, and Cosmetic Act:

Approval under this rule requires ... that the effect shown be, in the judgment of the agency, clinically meaningful, and of such importance as to outweigh the risks of treatment. This judgment does not represent either a "lower standard" or one inconsistent with section 505(d) of the act, but rather an assessment about whether different types of data show that the same statutory standard has been met.¹⁴

Further to this point, in a statement on October 17, 2017, FDA Commissioner Dr. Scott Gottlieb explained that "[FDA] sees] a product that goes through FDA's accelerated approval process as meeting the gold standard for approval" and that such drugs "meet a high hurdle for access to the market."¹⁵

In short, from 1992 to the present, Congress and FDA have repeatedly emphasized that therapies approved through the accelerated pathway must satisfy FDA's safety and effectiveness standards and must be covered by Medicaid in accordance with the Medicaid rebate statute. The 21st Century Cures Act was similarly designed to "ensure that our country remains on the forefront of medical innovation while maintaining the gold standard for approvals of medical products."¹⁶

Excluding drugs with only surrogate endpoint data ignores the science underlying accelerated approval

In targeting exclusion of drugs when "only surrogate endpoints have been reported", OHA fails to recognize that surrogate endpoints may be more reliable than clinical endpoints in detecting a measurable

¹² FDA, Guidance for Industry, Expedited Programs for Serious Conditions —Drugs and Biologics at 7 (May 2014)

¹³ 57 Fed. Reg. at 58945 (emphasis added). (referred to as "Expedited Pathways Guidance")

¹⁴ 57 Fed. Reg. at 58944.

¹⁵ FDA's Gottlieb Defends Accelerated Approval Pathway As Meeting Gold Standard, Watching For Access Limitations By Payors," Prevision Policy (Oct. 18, 2017).

¹⁶ July 10, 2015 Congressional Record at E1036 (statement of Rep. Pallone) (emphasis added).

benefit in some situations because slow, variable disease progression and small patient numbers may confound results that rely on clinical endpoints. Increased understanding about the causes of disease enables the selection of more relevant and reliable biomarkers that are directly related to both disease pathophysiology and the mechanism of drug action. This allows for a more accurate assessment of whether a drug is likely to have a beneficial treatment effect in a given disease.

Specific to Duchenne, a growing body of scientific evidence supports the use of dystrophin as a surrogate endpoint. The sole cause of Duchenne is well understood to be a lack of dystrophin. Exon-skipping therapies act directly upon this root cause to restore dystrophin production. And dystrophin can reliably be quantified by a validated assay. In approving the first exon skipping product for Duchenne, FDA concluded that “the biochemical data strongly support the idea that low-level increases in dystrophin product are reasonably likely to predict clinical benefit.”¹⁷ More recently, a team of independent clinical researchers conducted a study reinforcing the predictive value of dystrophin as a surrogate endpoint, demonstrating that dystrophin in very low quantities, as low as less than 1%, leads to an attenuated disease course, noting delayed time to loss of ambulation and declines in vital capacity and cardiac function, and improved survival compared to patients with no dystrophin.¹⁸ Today’s surrogate endpoints, like dystrophin, are not a leap of faith but grounded in science.

Excluding drugs approved through accelerated approval denies patients' access to cutting edge treatments for which limited or no alternatives exist and exacerbates health disparities

As written, Section 3.3, Strategy 3 could allow OHA to exclude not just accelerated approval drugs but most drugs, because the FDA’s drug approval framework does not require evidence of an “incremental benefit” over existing therapies for a demonstration of safety and efficacy.¹⁹ However, excluding accelerated approval drugs would particularly undermine the most vulnerable patients’ access to FDA-approved treatments for rare diseases where no other treatments may exist.

As you appreciate, Medicaid is critical for people with rare diseases, especially children, half of whom rely on the program for the care and treatment they need. Oregon’s own researchers from the Oregon Health & Science University (OHSU) collaborated with the National Institute of Health’s National Center for Advancing Translational Science and concluded in an October 2021 published study that there is an “urgent and considerable need for earlier and accurate rare disease diagnosis and intervention to address medical management for rare disease patients.”²⁰ Creating barriers that prevent access to rare disease treatments approved through accelerated approval runs counter to OHSU’s conclusions and could have devastating consequences for the health and well-being of Medicaid beneficiaries.

OHA’s Section 3.3, Strategy 3 proposal would be particularly harmful to adults with rare diseases. The unfortunate reality is that only half of patients with a rare disease will reach adulthood. Many such patients wait years for an FDA approved treatment to ever be available, meaning a Medicaid patient diagnosed as a child may be an adult when a treatment finally receives FDA approval. Conversely, an Oregon Medicaid patient may be prescribed and taking an accelerated approval drug as chronic treatment through adulthood. As we interpret OHA’s proposal, adult Oregon Medicaid patients would be blocked from continuing to

¹⁷ FDA, Center Director Decisional Memo. September 2016.

¹⁸ De Feraudy Y, Yaou RB, Wahbi K, et al. Very low residual dystrophin quantity is associated with milder dystrophinopathy. *Ann Neurol* 2020;; 1-13.

¹⁹ As noted earlier, the waiver request would define drugs with “limited or inadequate evidence of clinical efficacy” so that it would not just include accelerated approval drugs but also drugs “provid[ing] no incremental benefit within its therapeutic class, compared to existing alternatives.”

²⁰ Tisdale, A., Cutillo, C.M., Nathan, R. *et al.* The IDEaS initiative: pilot study to assess the impact of rare diseases on patients and healthcare systems. *Orphanet J Rare Dis* 16, 429 (2021). <https://doi.org/10.1186/s13023-021-02061-3>

access this treatment on their 18th birthday or never access a future treatment because of their age. Such an approach to healthcare is discriminatory and unethical and sends a strong message to Medicaid patients that their lives are not worth treating. More so, it will perpetuate drastic and life-threatening situations for patients who may have no other treatment options.

Excluding accelerated approval drugs will discourage future innovation

Excluding coverage for drugs approved under accelerated approval pathway will also discourage manufacturers from developing innovative therapies if substantial portions of the population will no longer be able to access those therapies after they are developed. This is especially true for rare diseases, as developing treatments for these diseases poses unique challenges,²¹ and the potential rewards for innovation (and rewards for society, i.e., patient access) dwindle if the already-small patient population effectively gets smaller due to payors targeting novel treatments for coverage restrictions.

The accelerated approval pathway is a critical regulatory pathway that enables and encourages development of medicines for rare and ultra-rare diseases. It can serve as an important tool in the innovation cycle – enabling the development of the first treatment for a rare disease, providing patients access, and spurring additional investment and competition in the development of subsequent treatments. This is exactly what has unfolded in Duchenne. Sarepta invested approximately \$2 billion in research and development over more than a decade to advance our Duchenne exon-skipping RNA therapeutic pipeline, leading to the first FDA-approved treatment for Duchenne, EXONDYS 51, in 2016. Accelerated approval of EXONDYS 51 enabled not only Sarepta to reinvest our revenue and more back into developing additional and improved innovations for Duchenne patients (~2/3 of our budget is allocated to research and development year over year), but it also signaled to the broader industry that a viable regulatory pathway to approval exists for this complex, rare disease. The approval catalyzed unprecedented investment and innovation in Duchenne, leading to a transformed treatment landscape with 5 FDA-approved therapies, more than 30 treatments in the pipeline, including next-generation exon-skipping therapies, gene therapy and gene editing approaches, and over 25 companies in the space today.²² Notably, of RNA therapies in development dystrophin is the most common target and Duchenne ranks among the most common diseases being studied for RNA and gene therapies.²³ The accelerated approval pathway can be credited for these advances and enabling the first step to forever changing the course of Duchenne. Formulary restrictions targeting accelerated approval drugs could disrupt this cycle, deter future development of treatments for deadly and otherwise serious diseases, limit choices for patients and their physicians, and hinder competition.

OHA's waiver thwarts the aims of the Food, Drug, and Cosmetic Act and undermines FDA's statutory role in determining drug safety and effectiveness

As proposed, Section 3.3, Strategy 3 would thwart the goals of the Federal Food, Drug and Cosmetic Act (FDCA), which tasks FDA with applying its expertise to speed the development of medicines for serious

²¹ For example, the FDA has noted that rare diseases create the following research challenges differing from other diseases: (1) "small populations, limited opportunity for study and replication in clinical trials"; (2) "highly heterogeneous collection of diseases" ("e.g., genetic disorders often characterized by wide range of severity, clinical presentation and rate of progression"); (3) "diseases are poorly understood" ("natural histories incompletely described" and "diagnosis difficult"); (4) "most are serious or life-threatening, most have unmet medical needs" (thus "lack[ing] regulatory/drug development precedent"); (5) "endpoints, outcome assessment tools often lacking"; and (6) "many affect pediatric patients" (thus posing "additional ethical considerations and constraints"). "Rare Diseases and Clinical Trials," presentation by Anne Pariser, MD, Office of Translational Sciences, Center for Drug Evaluation and Research, FDA (Nov. 4, 2014) at 6.

²² PPMD. Duchenne Drug Development Pipeline. Accessed December 13, 2021. <https://www.parentprojectmd.org/duchenne-drug-development-pipeline/>

²³ American Society of Gene and Cell Therapy. Q3 2021 Quarterly Data Report. Gene, Cell & RNA Therapy Landscape. Available at: <https://asgct.org/global/documents/asgct-pharma-intelligence-quarterly-report-q3-2021.aspx>

diseases while maintaining its rigorous approval standards. As explained in the extensive findings and sense of Congress provisions of FDASIA 901 —

[FDA] serves a critical role in helping to assure that new medicines are safe and effective. Regulatory innovation is 1 element of the Nation's strategy to address serious and life-threatening diseases or conditions by promoting investment in and development of innovative treatments for unmet medical needs.

* * *

...FDA should be encouraged to implement more broadly effective processes for the expedited development and review of innovative new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions, including those for rare diseases or conditions, using a broad range of surrogate or clinical endpoints and modern scientific tools.

* * *

The [pre-FDASIA] statutory authority governing expedited approval...should be amended...to expedite development and access to novel treatments for patients with a broad range of serious or life-threatening diseases or conditions.

FDA has emphasized the importance of tools like the accelerated approval pathway in realizing FDA's statutory mandates. As a 2015 FDA white paper explained:

The statutory requirement for approving a new drug is that it be shown to be safe and effective. Effectiveness must be based on substantial evidence from adequate and well-controlled clinical investigations. This requirement usually means evidence from at least two adequate and well controlled studies, each convincing on its own, although a single study can be sufficient. The agency "exercise[s] the broadest flexibility in applying the statutory standard, while preserving appropriate guarantees for safety and effectiveness," as its regulations state...

* * *

Nowhere is the use of flexibility in drug development more evident -and impactful - than in the case of rare, or "orphan," diseases that afflict a small percentage of the population[F]inding effective treatments for rare diseases is a public health priority, and FDA has brought to bear all of its drug review and technical assistance tools to assist the development of new treatments for these conditions."²⁴

FDA's leaders have recognized that achieving this mission requires collaboration with FDA's sister agencies and Congress to speed the development of innovative treatments that meet FDA's exacting standards. As Dr. Robert Califf, FDA's Commissioner from 2016-17, explained:

With [the 21st Century Cures Act], great progress has been made towards our shared goal of advancing regulatory science so that we can continue to speed the discovery, development, and delivery of medical products to prevent and cure disease and

²⁴ FDA White Paper, FDA and Accelerating the Development of New Pharmaceutical Therapies, 7-8 (March 23, 2015).

improve health while sustaining the evidence framework that enables assurance to the public of the safety and effectiveness of medical products.

FDA now stands ready to work with Congress, our sister federal agencies and the medical products ecosystem to implement these important provisions as we continue to work on behalf of all Americans to protect and promote public health and promote innovation...²⁵

OHA's Section 3.3, Strategy 3, if granted, would disrupt this statutory framework. Even though the FDCA already establishes a robust framework for FDA's expert review and approval of safe and effective medicines, the OHA suggests that drugs granted accelerated approval "would be ideal for more rigorous evaluation" and seeks "authority to limit [OHP's] formulary to exclude unproven or low-value drugs".²⁶ Further, OHA implies Oregon is more equipped to "use its own rigorous review process to determine coverage of new drugs and to prioritize patient access to clinically proven, effective drugs"²⁷ than the FDA.

Such an approach by Oregon would diminish FDA's statutory role as the expert gatekeeper entrusted by Congress to determine the safety and efficacy of new drugs and would limit FDA's effectiveness in speeding innovative treatments to seriously ill patients with unmet needs. Further, the review would be led by an organization (OHA) that has historically tried to block access to accelerated approval drugs. In 2017, OHA's Health Evidence Review Commission (HERC) assigned EXONDYS 51 to a newly created unfunded line of the Prioritized List, line 660, for "conditions for which certain treatments have no clinically important benefit" and then retracted this approach after Sarepta challenged Oregon's legal authority as it conflicted with federal drug coverage requirements.²⁸ OHA has demonstrated repeated skepticism regarding the clinical merits of drugs approved via the accelerated pathway, reflecting a strong bias, and as such will not conduct a review with the same objectivity as the rigorous review as executed by FDA in its approval of these drugs.

The requested waiver would also generate regulatory redundancy and inefficiency, as OHA would be carrying out functions that have already been assigned to—and already have been carried out by—a federal agency, effectively adding another layer of review for product developers. This is just the opposite of what a Medicaid demonstration should be doing; waivers should eliminate redundancy and create efficiency, streamlining processes of product review rather than adding costly and time-consuming new layers that further delay treatments from getting to patients.

Section 1115 cannot be interpreted to permit this waiver. When potential conflicts exist between two federal statutes, courts must apply "the familiar canon" of adopting "the interpretation that preserves the principal purposes of each."²⁹ If the two laws cannot be harmonized (and do not specifically address the

²⁵ 215 Century Cures Act; Making Progress on Shared Goals for Patients, FDA Commissioner Dr. Robert M. Califf, FDA Voice, December 13, 2016.

²⁶ Oregon 1115 Medicaid Demonstration Waiver – Draft Application for Public Comment 12/1/2021

²⁷ Oregon 1115 Medicaid Demonstration Waiver – Draft Application for Public Comment 12/1/2021

²⁸ In May 2018, OHA retracted EXONDYS 51's assignment recognizing "federal requirements set out in section 1927 of the Social Security Act (the federal Medicaid rebate law) and Oregon's 1115 Medicaid Demonstration Waiver, we are not going to pursue this approach further at this time." Oregon Health Authority. Prioritization of FDA-approved drugs on unfunded lines of the Prioritized List. May 14, 2018.

²⁹ SmithKline Beecham Consumer Healthcare, LP v. Watson Pharmaceuticals, Inc. 211 F.3d 21, 27-28 (2d. Cir. 2000). See also, *te c ., Vomado Air Circulation Systems, Inc. v. Duracraft Corp.*, 58 F.3d 1498, 1507 (10th Cir. 1995) ("Except to the extent that Congress has clearly indicated which of two statutes it wishes to prevail in the event of a conflict, we must interpret and apply them in a way that preserves the purposes of both and fosters harmony between them"); *Zenith Electric Corp. v. Exzec, Inc.*, 182 F.3d 1340, 1347 (Fed. Cir.

resolution of conflicts), then courts give effect to the law that was enacted most recently or that more specifically addresses the matter at issue.³⁰

These interpretive principles all dictate the same result here: Section 1115 must be interpreted to harmonize with the FDCA's accelerated approval provisions and this waiver request cannot be approved. To do otherwise would conflict with both the FDCA and the Medicaid rebate statute (which gives great weight to FDA approval decisions, requiring that State Medicaid programs generally cover rebated drugs when used for "medically accepted indications," including "any use for a covered outpatient drug which is approved under the Federal Food, Drug and Cosmetic Act").³¹ There is no exception to this requirement for accelerated approval drugs: FDA applies a single overarching approval standard that all approved medicines must meet, regardless of whether they were approved via the traditional or accelerated pathway.

The principal purpose of Section 1115, which was enacted in 1962 and applies to programs authorized under six different titles of the Social Security Act, is allowing States to "test out new ideas and ways of dealing with the problems" of program beneficiaries.³² Congress "intended that the Secretary would 'selectively approve[]' state projects" and the HHS Secretary "has plenary authority to reject State projects and to require States to modify projects to make them more consistent with federal requirements, less likely to harm recipients, and more likely to further the goals of the Social Security Act."³³ Thus, CMS is not obliged to grant a waiver that would undercut a sister agency's ability to carry out its statutory mission and harm beneficiaries who need access to safe and effective, FDA-approved new therapies. Section 1115 is a broad provision that does not deal with the matter at issue here and its purpose would not be implicated by denying this waiver; it is difficult to believe Congress ever envisioned Section 1115 being used for such a purpose. By contrast, this waiver would sharply limit FDA's ability to achieve the principal purposes of the FDCA's accelerated approval provisions—which were enacted in 2012, decades after the enactment of Section 1115, and are directly targeted by this waiver request. In these circumstances, Section 1115 cannot permissibly be interpreted as allowing the waiver OHA requests.

2. Fails to meet the requirements under the federal Social Security Act (SSA) section 1115 and Oregon's obligations under the Medicaid Drug Rebate Statute (SSA section 1927)

OHA's closed formulary approach and exclusion of accelerated approval drugs violates the principal tenets of the Medicaid drug rebate program and purpose of 1115 demonstration authority Beyond impermissibly setting up a conflict with the FDCA, Oregon intends to request CMS to waive the Medicaid rebate statute's drug coverage requirements (specifically, Social Security Act (SSA) § 1927(d)(1)(B)). The Medicaid rebate statute requires drug manufacturers to pay large rebates on Medicaid utilization of their products, in exchange for state Medicaid programs covering that product subject only to the "permissible restrictions" specified in the rebate statute. In 2018 guidance to state Medicaid programs, the CMS reinforced "drugs that are granted 'accelerated approval' are drugs approved by FDA under section 505(c) of the FDCA [Federal Food, Drug and Cosmetic Act], and are able to satisfy the definition of covered outpatient drug, and if used for a medically-accepted indication, then the drug must

1999) (same); *FMC Corp. v. Control Solutions, Inc.*, 369 F. Supp.2d 539, 571 (E.D. Pa. 2005) (statutes in conflict should be interpreted to preserve "principal purpose" of each, but no conflict between two statutory regimes existed where "the EPA regulations do not explicitly require copying [in violation of the Copyright Act] of the original and pioneer label and the applicable statutes and regulations here do not intimate such a result"); *IRIS Corp. v. Japan Airlines InYI Co.*, 2009 WL 3245910, *4 (E.D. N.Y. 2009) (following the SmithKline framework of preserving the "principal purposes" of two conflicting statutes).

³⁰ See, e.g., *Hawaii v. Trump*, 859 F.3d 741, 778 (9th Cir. 2017) ("a later-enacted, more specific statute generally governs over an earlier, more general one").

³¹ Social Security Act § 1927(k)(6), (d).

³² S. Rep. No. 1589, 87th Cong., 2d Sess. 20, re printed in 1961 U.S.C.C.A.N. 1943, 1961.

³³ *Beno v. Shalala*, 30 F.3d 1057, 1069 (9th Cir. 1994) (citing S. Rep. 1589 at 20).

be covered by state Medicaid programs if the manufacturer has an applicable signed Medicaid national drug rebate agreement for participation in the MDRP [Medicaid Drug Rebate Program].”³⁴ OHA requests that CMS waive these coverage requirements and allow Oregon to establish a closed formulary without the safeguards the rebate statute requires of a Medicaid formulary. Oregon is pursuing this request, despite CMS’s denial of MassHealth’s³⁵ similar attempt to establish a closed formulary upon which Oregon modeled its 1115 waiver.

OHA’s waiver cannot be approved for several reasons:

First, SSA § 1927 (the Medicaid rebate statute) cannot be waived under Section 1115.³⁶ In *PhRMA v. Thompson*, a ruling that has never been overturned or questioned by later cases, the D.C. Circuit held that:

The Social Security Act, of which the Medicaid statute is a part, authorizes HHS to approve experimental "pilot" or "demonstration" projects that the Secretary determines are "likely to assist in promoting the objectives of [Medicaid]." [42 U.S.C.] § 1315(a) [Social Security Act § 1115(a)]. Although the Act authorizes the Secretary to waive certain Medicaid requirements for such demonstration projects, it does not authorize him to waive any requirements of [42. U.S.C.] Section 1396r-8's [SSA 1927's] rebate provision, . . . See id. § 1315(a)(1).³⁷

Second, even if CMS could waive the requirements of the Medicaid rebate statute under section 1115, it still could not selectively waive the rebate statute's coverage requirements, while leaving in place the requirement for manufacturers to pay rebates. The rebate statute's legislative history emphasizes that the statute is a carefully-constructed package with inseparable parts:

The Committee believes that Medicaid, the means-tested entitlement program that purchases basic health care for the poor, should have the benefit of the same discounts on single source drugs that other large public and private purchasers enjoy. The Committee bill would therefore establish a rebate mechanism in order to give Medicaid the benefit of the best price for which a manufacturer sells a prescription drug to any public or private purchaser. Because the Committee is concerned that Medicaid beneficiaries have access to the same range of drugs that the private patients of their physicians enjoy, the Committee bill would require States that elect to offer prescription drugs to cover all of the products of any manufacturer that agrees to provide price rebates.³⁸

³⁴ CMS Medicaid Drug Rebate Program Notice, Release No. 185. State Medicaid Coverage of Drugs Approved by the FDA under Accelerated Approval Pathway. June 27, 2018.

³⁵ CMS Response to MassHealth Regarding 1115 waiver demonstration request, June 27, 2018.

³⁶ SSA § 1115(a)(1) provides that, "[i]n the case of any experimental, pilot, or demonstration program which, in the judgment of the Secretary, is likely to assist in promoting the objectives of [Medicaid or certain other programs], in a State or States -- (a) the Secretary may waive compliance with any of the requirements of section 402, 454, 1402, 1602, or 1902 ... to the extent and for the period he finds necessary to enable such State or States to carry out such project."

³⁷ *PhRMA v. Thompson*, 251. F.3d 219, 222 (D.C. Cir, 2001) (emphasis added).

³⁸ H. Rpt. 101-881, 101st Congress, 2d Session (Oct. 16, 1990) (emphasis added).

Thus, the rebate statute is a "government-industry compact"³⁹ that purposely coupled the rebate requirements on manufacturers with the coverage requirements on States.⁴⁰ As the Supreme Court has emphasized, "strict adherence to the language and structure of an act is particularly appropriate where ... a statute is the result of a series of carefully crafted compromises."⁴¹ Many cases reinforce this point, holding that a statute reflecting a legislative bargain must be interpreted to uphold that bargain.⁴² The rebate statute is just such a legislative bargain and CMS cannot authorize a State to keep the benefits of the bargain without fulfilling its coverage obligations.⁴³

Third, the waiver Oregon seeks does not meet the requirement that 1115 waivers must promote Medicaid objectives.⁴⁴ The Medicaid statute generally describes Medicaid's objectives as providing medical assistance to those whose income and resources are inadequate to meet the costs of such care.⁴⁵ Instead of enabling states to assist people who cannot afford necessary medical care, Section 3.3 Strategy 3 could restrict beneficiaries' access to medicines and adversely affect their health in two important ways: by permitting Oregon to cut back on drug coverage, particularly for innovative drugs approved through FDA's accelerated approval pathway; and by reducing manufacturers' incentive to develop innovative treatments in the future (and potentially by reducing their incentive to participate in the Medicaid rebate program) if the waiver were to be approved and then replicated in other states.

Congress meant for the Medicaid rebate statute to assure Medicaid patients access to "the same range of drugs as private patients of their physicians enjoy,"⁴⁶ and has repeatedly emphasized the vital role that innovative treatments that are granted accelerated approval play in this nation's healthcare. Section 3.3 Strategy 3 of OHA's waiver request conflicts with both of these goals and it would set back Medicaid objectives rather than promote them.

Finally, because section 1115 only permits "experimental, pilot, or demonstration projects," the courts require that these projects have legitimate research value—they must be designed to learn something new and not just to reduce spending or to replicate benefit cuts that have well-known effects. But there is nothing in the waiver request to suggest that OHA's closed formulary proposal is designed to generate knowledge or would do so. The closed formulary strategy with exclusions for accelerated approval drugs as described in section 3.3 appears to be positioned by OHA as a means merely to cut benefits and reduce spending.

³⁹ Medicare and Medicaid Reconciliation: Hearings Before the Subcomm. on Health and the Environment of the Committee on Energy and Commerce, H. Hrg. 103-61, 103rd Cong. 453 (1993) (statement of Rep. Waxman).

⁴⁰ The standard Medicaid Rebate Agreement that implements the rebate statute, drafted by CMS shortly after the statute's enactment, thus details the manufacturer's obligations to calculate and pay Medicaid rebates and recognizes that manufacturers must be able to rely on CMS to enforce the statute's coverage obligations, providing that "a State's failure to comply with the drug access requirements of section 1927 shall be cause for the manufacturer to notify CMS and for CMS to initiate compliance action against the State." Medicaid Rebate Agreement § VI(a).

⁴¹ *Community for Creative Non-Violence v. Reid*, 490 U.S. 730, 748 n.14 (1989).

⁴² See, e.g., *General Motors Corp. v. Romein*, 503 U.S. 181, 191 (1992) (upholding statutory provisions necessary to "preserve the delicate legislative compromise that had been struck by [prior] laws"); *Rodriguez v. Compass Shipping Co.*, 451 U.S. 596, 612 (1981) ("[in] interpreting the intent of Congress in fashioning various details of this legislative compromise, the wisest course is to adhere closely to what Congress has written."); *Mohasco Corp. v. Silver*, 447 U.S. 807, 826 (1980) ("We must respect the compromise embodied in the words chosen by Congress. It is not our place simply to alter the balance struck by Congress").

⁴³ The waiver request also fails to acknowledge that the rebate statute already gives States significant flexibility, permitting States to exclude or otherwise restrict coverage in a variety of circumstances.

⁴⁴ Social Security Act § 1115(a).

⁴⁵ Social Security Act § 1901.

⁴⁶ H. Rpt. 101-881 (Oct. 16, 1990).

3. Falls far short of meaningful cost containment given drugs approved through this pathway are not a primary driver of Medicaid spending or its growth, particularly when weighed against significant potential harm to patients

Targeting accelerated approval drugs will not yield significant budget savings

OHA presents its Section 3.3, Strategy 3 proposal as cost savings stating “the state could avoid exorbitant spending on high-cost drugs that are not medically necessary” but does not point to specific data identifying the impact of accelerated approval drugs on OHA’s budget. A recent publication sheds light on the budget impact of these drugs, demonstrating they are not a key driver of Medicaid spending. Data indicate that accelerated approval drugs account for less than 1% of annual Medicaid spending consistently year over year (2007-2018).⁴⁷ Notably, Medicaid spending on accelerated approval drugs did not increase but instead remained steady at 0.6-0.8 percent per year after 2012 passage of the Food and Drug Safety and Innovation Act (Section 901), which enhanced the accelerated approval pathway and encouraged its broader use for rare diseases. Over the 2007 to 2018 period, hospital spending contributed the most to Medicaid spending and its growth, accounting for nearly 30% of program expenses. Targeting accelerated approval drugs is misdirected as it will not yield meaningful savings for OHA but instead threatens to harm the state’s most vulnerable beneficiaries.

* * *

For the reasons noted above, we respectfully request OHA to not move forward with Section 3.3 Strategy 3 of its 1115 waiver proposal to establish a closed prescription drug formulary and exclude accelerated approval drugs. As outlined, the accelerated approval pathway is a crucial and irreplaceable tool for diseases for which approval via the traditional pathway is not feasible for practical, scientific, or ethical reasons. If Section 3.3 Strategy 3 is implemented as proposed, OHA would not meet the objectives of their 1115 waiver proposal to achieve health equity and instead would further marginalize the state’s safety-net population, including patients with rare diseases and the disabled population. We hope OHA considers these implications and, instead, focuses on implementing policies that facilitate health equity, recognize FDA as the sole authority for determining safety and effectiveness of medical products, and uphold the purpose of the Medicaid drug rebate program which is to ensure all patients have access to FDA approved drugs for which their treating physicians deem medically necessary.

If you have questions, please contact me at dberry@sarepta.com or 425-905-8377.

Sincerely,



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SVP, Global Policy, Government & Patient Affairs

Cc: Patrick Allen, Director of the Oregon Health Authority (OHA)

⁴⁷ Thorpe, K. and Holtz-Eakin D. Quantifying Impact of Accelerated Approval Drugs on Medicaid Spending. *American Journal of Managed Care*. 30 Mar 2021