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Subject: Comment Regarding Application A.24 Risdiplam for the Treatment of Spinal Muscular Atrophy

To the WHO EML Secretariat and Expert Committee on Selection and Use of Essential Medicines:

I am writing to express my support for the proposal to add risdiplam to the WHO Model Lists of Essential Medicines.

I am a pediatric neurologist who has specialized in treatment of neuromuscular conditions for my three-decade career, with a particular interest in spinal muscular atrophy (SMA). SMA is a devastating condition that is estimated to impact 1 out of 11,000 newborns.[1] It is an inherited disease for which families with 2 carrier parents have a 1 in 4 chance of having an affected child, and it is estimated that roughly 1 in 50 adults is a carrier.[2] The rapid degeneration of nerve cells that causes the severe clinical features of SMA often begins before birth.[3] When left untreated, it is the leading genetic cause of death in infants.[4] Children with the most common type of SMA, those with early infantile onset, will generally die of respiratory failure before their second birthday without treatment.[5] If the disease is not suspected due to family history or detected on a screening test, it will not be diagnosed in time to maximize benefits of current disease modifying treatments (DMT).

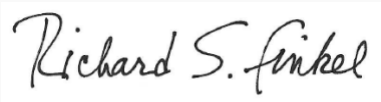
Screening for SMA is efficient with the proper diagnostic equipment and clinical infrastructure, and it has been made more accessible in recent years via availability and use of kits and centralized genetic testing (quantitative PCR). When DNA testing for some genetic forms of immunodeficiency (SCID and XLA) is already being performed, it is easy to add SMA to the program. The test requires only a dried blood spot commonly obtained shortly after birth with a simple heel prick and can produce results in a matter of a few days. However, without available treatment options for SMA, the impact of early detection on long-term patient survival is significantly tempered.

For years, I have worked with pharmaceutical companies to develop and lead clinical trials that have established safety and efficacy data to gain regulatory approvals for SMA treatments, including Evrysdi® (risdiplam), SPINRAZA® (nusinersen), and ZOLGENSMA® (onasemnogene abeparvovec-xioi). The availability of these treatments has transformed clinical care and treatment and survival rates for SMA throughout the world over the last decade.

Risdiplam has been proven in longitudinal studies to prolong survival and safely ameliorate manifestations of SMA in affected patients compared to untreated patients.[6] Patients identified shortly after birth and treated pre-symptomatically have been shown to achieve even more robust responses to these DMTs—achieving major motor milestones (e.g. walking) as well as independent feeding and breathing[7, 8]—feats that are impossible for this same population without treatment. In addition to the obvious impact of treatment on patient survival and function, risdiplam therapy also reduces the burden of providing supportive care for these patients, saving health systems and payors over the long-term.

In collaboration with St. Jude Global, I am engaging clinician and advocacy partners around the world to invest in supporting improvement of SMA care in low- and middle-income countries (LMICs). We are working to expand access to newborn and other screening technology that can be used to detect SMA and allow for the earliest possible intervention and best long-term patient outcomes. Risdiplam is an attractive global treatment option due to its ease of oral administration in both reconstituted liquid and tablet forms and its shelf stability, in addition to its safety and efficacy. The inclusion of risdiplam on the EML will allow for greater awareness of and access to SMA treatment options that may not yet be available in LMICs.

Sincerely,



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