Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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MEDIA & INVESTOR RELEASE

FDA approves Novartis Vijoice® (alpelisib) as first and only treatment for select patients with PIK3CA-Related Overgrowth Spectrum (PROS)

- *Vijoice is first approved treatment to specifically address the root cause of PROS conditions in select patients 2 years of age and older*[1]
- *PROS is a spectrum of rare conditions and is characterized by atypical overgrowths and anomalies in blood vessels, the lymphatic system and other tissues*[2,3]
- *Approval based on real-world data from EPIK-P1 study, which showed patients treated with Vijoice experienced reduction in the size of PROS lesions and improvement of PROS-related signs and symptoms*
- *Novartis to offer robust patient support program that includes assistance to access medication, financial resources for eligible patients and continued education*

Basel, April 6, 2022 — Novartis today announced that the U.S. Food and Drug Administration (FDA) granted accelerated approval to Vijoice® (alpelisib) for the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA-Related Overgrowth Spectrum (PROS) who require systemic therapy.[1] Vijoice is the first FDA-approved treatment for PROS, a spectrum of rare conditions characterized by overgrowths and blood vessel anomalies impacting an estimated 14 people per million.[2,3] In accordance with the Accelerated Approval Program, continued approval may be contingent upon verification and description of clinical benefit from confirmatory evidence.

“Today’s approval of the first treatment for PROS offers hope for a better quality of life to patients and families affected by these rare conditions,” said Kristen Davis, Executive Director of CLOVES Syndrome Community. “PROS conditions can be debilitating and disabling and can result in disruptions to everyday activities. Until today, often the only treatment options for patients were surgical or interventional radiology procedures.”

PROS conditions can affect quality of life and pose a range of physical, emotional and social challenges for patients and their families, ranging from functional impacts and developmental delays to chronic pain, mobility issues, and feelings of isolation.[3-6] PROS management can be challenging, requiring collaboration from a multidisciplinary team, and patients and physicians have only had access to interventions focused on symptom management.[6,7]

“I am proud of this outstanding achievement for the PROS community. The EPIK-P1 study results build on our earlier pre-clinical findings and demonstrate the efficacy of Vijoice for select PROS conditions, effectively reducing PROS growths,” said Guillaume Canaud, MD,

PhD, Necker-Enfants Malades Hospital – AP-HP, the Paris Descartes University, Inserm (INEM Institute Necker Enfants Malades – Centre for Molecular Medicine). “This is a significant advancement in therapy for PROS with the potential to positively change the treatment trajectory and outcomes for patients.”

FDA approval was based on real-world evidence from EPIK-P1, a retrospective chart review study that showed patients treated with Vijoice experienced reduced target lesion volume and improvement in PROS-related symptoms and manifestations. The primary endpoint analysis conducted at week 24 showed 27% of patients (10/37) achieved a confirmed response to treatment, defined as 20% or greater reduction in the sum of PROS target lesion volume. Nearly three in four patients with imaging at baseline and week 24 (74%, 23/31) showed some reduction in target lesion volume, with a mean reduction of 13.7%, and no patients experienced disease progression at time of primary analysis. Additionally, at week 24, investigators observed patient improvements in pain (90%, 20/22), fatigue (76%, 32/42), vascular malformation (79%, 30/38), limb asymmetry (69%, 20/29), and disseminated intravascular coagulation (55%, 16/29). These improvements were observed in subsets of patients across the study population (n=57) who reported symptoms at baseline and at week 24.[1,2]

“The approval of Vijoice marks a turning point for patients who, until now, have not had an approved therapy to specifically address their disease,” said Victor Bulto, President, Novartis Innovative Medicines US. “We are grateful to the physicians, patients and families who participated in the EPIK-P1 trial. We are continuing to invest in studies to advance the scientific understanding of PROS conditions and to understand the full potential of Vijoice.”

In EPIK-P1, the most common adverse events (AEs) of any grade were diarrhea (16%), stomatitis (16%), and hyperglycemia (12%). The most common grade 3/4 AE was cellulitis (4%); one adult case was considered treatment-related.[1]

Novartis is committed to providing patients with access to medicines, as well as resources and support to address a range of needs. The Novartis Oncology Patient Support Program is available to help guide eligible patients through the various aspects of getting started on treatment, from providing educational information to helping them understand their insurance coverage and identify potential financial assistance options. Patients or providers can call 800-282-7630 or visit Patient.NovartisOncology.com or HCP.Novartis.com/Access to learn more about eligibility and to enroll.

About PIK3CA-Related Overgrowth Spectrum (PROS)
The PROS classification was proposed by researchers and parent representatives of patient-family support and advocacy organizations at a National Institutes of Health workshop in 2013 to unite a group of rare overgrowth conditions caused by PIK3CA mutations.[4,6] Specific conditions associated with PROS include KTS, CLOVES syndrome, ILM, MCAP/M–CM, HME, HHML, FIL, FAVA, macrodactyly, muscular HH, FAO, CLAPO syndrome and epidermal nevus, benign lichenoid keratosis, or seborrheic keratosis.[4,6] The estimated prevalence of PROS conditions is approximately 14 people per million.[3]

About Vijoice
Vijoice® (alpelisib) is a kinase inhibitor that treats rare overgrowth conditions caused by the effects of PIK3CA mutations in adults and children with PIK3CA-Related Overgrowth Spectrum (PROS). Vijoice works by inhibiting the PI3K pathway, predominantly the PI3K-alpha isoform.[1] Vijoice is the first FDA-approved treatment for PROS conditions. Vijoice is not approved for use outside the United States.

FDA approval of Vijoice is based primarily on real-world evidence from the EPIK-P1 study. To further understand the long-term efficacy and safety of alpelisib in PROS, Novartis is conducting additional clinical trials. EPIK-P2 is a prospective Phase II multi-center study with a randomized, double-blind, upfront 16-week placebo-controlled period, and extension period

to evaluate the safety, the efficacy and pharmacokinetics of alpelisib to treat pediatrics and adults with PROS. EPIK-P3 is a Phase II study to assess long-term safety and efficacy of alpelisib in people with PROS who participated in EPIK-P1.

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About Novartis

Novartis is reimagining medicine to improve and extend people’s lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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Novartis Media Relations
E-mail: media.relations@novartis.com

Anja von Treskow
Novartis External Communications
+41 79 392 86 97
anja.von_treskow@novartis.com

Dan Connelly
Novartis Oncology Communications
+1 862 210 0217
daniel.connelly@novartis.com

Julie Masow
Novartis US External Communications
+1 862 579 8456
Julie.masow@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 345 4440
Nicole Zinsli-Somm	+4 16 132 43809	Alina Levchuk	+1 862 778 3372
Isabella Zinck	+41 61 324 7188	Parag Mahanti	+1 973 876 4912