Novartis Position on Post-Trial Access[1]

The mission of Novartis is to discover new ways to improve and extend people's lives. Using science-based innovation, Novartis aims to deliver better outcomes for patients and to address society's evolving healthcare needs.

Clinical trials are an important part of the development and registration of innovative products, enabling the collection of robust safety and efficacy data on investigational products to support regulatory approval. This is only possible due to the patients who participate in our trials to further research and development. By virtue of participation, a patient may receive a new therapy during the clinical trial.

However, there are circumstances when on trial completion a patient who has derived clinical benefit from a product during the trial will need to continue to receive it. For example, there is a time lag between a patient completing a trial and product approval (or local patient access[2]), during which the product is not yet commercially available. In such instances, the product may need to be provided to trial participants who are deriving benefit, especially when no alternative or satisfactory treatment options are available to address their needs.

At Novartis, "Post-Trial Access" (PTA) refers to the provision of a product, either investigational treatment or comparator, to clinical trial participants following trial completion**.**

Novartis Position

At Novartis, we believe that we have an ethical responsibility to provide post-trial access free-of charge to all patients who participate in and complete a confirmatory[3] Novartis-sponsored clinical trial[4] until the product is commercially available and accessible locally[5] if[6]:

- There is evidence of continued clinical benefit for the patient and the patient consents to continue with treatment, and
- There are no comparable or satisfactory alternative treatment options available or a change in treatment poses a risk to the patient,[7] and
- Such provision is permitted as per local laws and regulations.

As already affirmed in the Novartis Commitment to Patients and Caregivers, our PTA principles are aligned with those in international ethical frameworks including the Declaration of Helsinki[8], the ICH Good Clinical Practices[9], and other international guidelines such as CIOMS[10] and UNESCO's Universal Declaration on Bioethics and Human Rights[11].

Moving forward, we will describe the post-trial access provision in all our clinical trial protocols and the related patient informed consent form, so patients are fully aware prior to agreeing participation in a study.

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When trial results have shown superiority of the Novartis investigational product to the comparator, we will offer the investigational product to all trial participants until the product is commercially available or accessible to these patients locally.

We also commit to consider exceptions on a case-by-case basis.

The complex and variable nature of studies and considerations for post-trial access means that we cannot anticipate and plan for all situations. In order to address the post-trial treatment needs of patients who have participated in Novartis-sponsored trials as quickly as possible, Novartis will ensure a process is in place to support prompt and fair decision-making and ensure a consistent approach across the world in compliance with applicable local laws and regulations.

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[1] Post-Trial access refers to individuals who did participate in a clinical trial. In contrast, expanded access or compassionate use [Novartis' "Managed Access"] is directed to individuals who cannot participate in a clinical trial. Post-Trial access is the sponsor's provision of investigational product for clinical trial participants after their trial participation ends. Post-Trial access may include open-label trial extensions, rollover studies, separate protocols, or protocol amendments.
[2] "Accessible to patient" means payor coverage or reimbursement in place, or a local access mechanism available (especially for self-paying markets).
[3] Confirmatory clinical trials are defined in ICH guideline E9 as "adequately controlled trials in which the hypotheses are stated in advance and evaluated." Confirmatory clinical trials are generally done after preliminary trials have provided an early signal of efficacy and are large enough to quantify the size of the beneficial and adverse effects.
[4] For conditions which are serious and/or life threatening, PTA may be provided earlier in the development lifecycle e.g. post proof of concept (post-POC) or following early exploratory trials, even without a fully elucidated safety and efficacy profile. Novartis will determine with the investigator evidence of benefit on a case-by-case basis for those trial participants with serious/life threatening conditions.
[5] "Commercially available" means local health authority approval and product launched.
[6] The provision by Novartis may be discontinued in certain instances e.g. if the program is terminated and the product is no longer manufactured, or if product is divested.
[7] For certain conditions it would be appropriate for the trial participant to transition to a therapy already approved for the indication. If withdrawal of the investigational treatment could lead to substantial harm or relapse, then it would be reasonable to continue that investigational treatment, even if alternative marketed therapies are available.
[8] Declaration of Helsinki (World Medical Association) (2013) and the United States (US) Belmont Report (1979).
[9] International Council for Harmonisation (ICH) E6: Guideline for Good Clinical Practice (GCP) (1996).
[10] International Ethical Guidelines for Biomedical Research Involving Human Subjects issued by the Council for International Organizations of Medical Sciences (CIOMS 2016).
[11] The Universal Declaration on Bioethics and Human Rights adopted by the United Nations Educational, Scientific, and Cultural Organisation (UNESCO) (2005).