Additional Discussion Questions and Answers: Public Meeting on the Development of a Public-Private Partnership Developing Anti-Cancer Therapies for Ultra-Rare Tumor Indications

The Foundation for the National Institutes of Health (FNIH)
National Cancer Institute (NCI)
FDA Oncology Center of Excellence (FDA OCE)

On August 24, 2023, the Foundation for the National Institutes of Health (FNIH), the National Cancer Institute (NCI), and the U.S. Food and Drug Administration Oncology Center of Excellence (FDA OCE) conducted a virtual meeting to discuss plans for creating a public-private partnership (PPP) to guide and support the development of new treatments for patients with ultra-rare cancers. Many pediatric and adult ultra-rare cancers have actionable oncogenic drivers not present in more common cancers; however, there is limited economic incentive to encourage concerted and coordinated efforts to develop drugs for these ultra-rare cancers.

During this multi-stakeholder meeting, participants discussed options for a collaborative open-science, open-drug development process for targeted therapies for ultra-rare cancer indications. FNIH solicited feedback and suggestions from the ultra-rare cancer community on the proposed PPP plans and moderated a discussion to gauge interest and resources available for drug development in this arena.

This document provides a summary of questions and answers posed in the meeting chat that were not discussed in depth during the meeting presentations or the live panel. Please note that questions and responses have been edited and/or combined for conciseness and clarity.

How does the PPP intend to avoid competing with existing research pipelines from private companies or academic entities (universities/non-profits/research institutes)?

We hope to synergize with ongoing programs related to drug development for ultra-rare cancers and avoid competition with any groups who have identified a viable drug development pathway for a particular target. To this end, the PPP will continue to take into account public information and information that groups are willing to share about their efforts. Through feedback mechanisms such as this stakeholder meeting and the post-meeting survey, the PPP will cast a wide net in order to enhance our understanding of the current landscape.

Given the focus on ultra-rare tumors, it is likely the PPP would require international collaboration if it were to gather enough tumor and patient data to make a meaningful attempt at targetable drug development. How does the PPP intend to address this?

In order to streamline our first efforts, the PPP intends to primarily focus on US-based resources and initiatives to start. However, we agree that ultimately this effort should expand to include global participation. With this in mind, we invited a number of international groups to the meeting that have interest in this area, and we do hope to eventually find collaboration and synergy with their efforts.

Will the PPP consider therapeutic modalities other than drugs aimed at specific molecular targets – for instance, internally delivered radiation therapy, immunotherapies that do not target a specific molecular pathway, therapeutic medical devices, or combination therapies?

Due to the molecular drivers often found in rare tumors, drugs that work against those molecular targets may be a large focus of the PPP. However, depending on the ultra-rare tumor(s) selected for the initial pilot, the PPP may consider other approaches to treatment as well. The PPP and associated stakeholders will discuss the optimal way to target selected tumors at future Biology Interrogation and Drug Platform Conferences (BIDPC).

Will model development (such as patient-derived xenografts or organoids) be part of the PPP?

As there are already existing initiatives in this space, such as the NCI Patient-Derived Models Repository (PDMR) and the NCI Pediatric Preclinical In Vivo Testing (PIVOT), the PPP is unlikely to focus on model development unless absolutely critical to drug development for a selected ultra-rare cancer.

Will this PPP consider n-of-1 approaches to trial design or other forms of personalized medicine – for instance, development of a pipeline to test and match rare cancer patients to personalized therapy recommendations?

The primary focus of the PPP will be on specific molecular targets that could be applied to all patients diagnosed with the same ultra-rare cancer.

Would patients who develop resistance to standard of care be in scope for the focus of this PPP?

The PPP is unlikely to target populations who develop resistance to standards of care in non-ultra rare cancers, given that these resistance mechanisms are likely to be generalizable across cancers and thus economically viable. When formulating the scope for the PPP, however, we will

consider both unmet need and currently available therapies along with the biology of the identified target. As such, ultra-rare tumors that have developed resistance to standard of care may be in scope for the PPP, as may resistance mechanisms that are specific to rare drivers (e.g., specific fusions). This may also vary in each iteration of the PPP, depending on the target selected.

This meeting has highlighted a number of existing initiatives in the rare and ultra-rare tumor space. Is there a way that participation in these initiatives could be streamlined, and is this something the PPP could tackle?

In developing the PPP infrastructure, the goal would be to seamlessly advance projects utilizing existing resources for rapid drug development. That being said, part of the pilot phase will be determining the current bandwidth and additional resources needed at each of the existing initiatives, and balancing priorities with the prospect of a shrinking NIH budget going forward. The value of the PPP regardless will be to demonstrate how programs can be leveraged by stakeholders and it should utilize resources from existing programs. Because the design of the PPP requires thoughtful leveraging and coordination of multiple of these resources and efforts, we will strive to streamline participation by participants, as well as communications between them for use by the broader scientific community.

Can FDA comment on the fast-approaching end date of the pediatric priority review voucher incentive? Although the end date is not until 2026, this already affects decisions on development for some of the orphan and ultra-orphan pediatric indications.

The FDA acknowledges this concern. It may be appropriate to contact the appropriate Congressional representatives since decision-making with respect to renewal of this program is made by Congress.