TBCAB
GLOBAL TB COMMUNITY ADVISORY BOARD

To: Masanori Kawasaki, Global TB Project Leader

Cc: Ramesh Dass, Head of Clinical Development & Commercial Strategy, Tuberculosis
Natasa Lazarevic, International Project Lead, Medical Affairs
Manuela Mladenova, Associate Director, Alliance Management and Supply Chain
Masoud Dara, Senior Director, Global Health & Public Affairs

30th April, 2025

Open Letter: Request for Information and Urgent Appeal to Accelerate Compassionate Use Access to Quabodepistat

Dear Dr. Kawasaki and colleagues,

We commend Otsuka's continued commitment to tuberculosis (TB) research and development and engagement with the Global TB Community Advisory Board (TB CAB). As research-literate, community activists committed to supporting the development of and access to new technologies and interventions capable of improving TB diagnosis, prevention, and treatment, we understand the critical importance of new drugs like quabodepistat to address drug-resistant TB (DR-TB). We write to follow up on prior conversations between the TB CAB and Otsuka to request an update regarding Otsuka's plans and timelines for establishing a compassionate use program for quabodepistat.

A coalition of front-line clinical providers, civil society organizations, and impacted community members, including members of the Global TB CAB, have come together under the banner of the BETTER (Building Expertise Treating TB with Expanded Resistance) Project to highlight the dire need for pre-approval access to novel compounds like quabodepistat for individuals with limited treatment options due to extensively drug-resistant TB (XDR-TB). The BETTER Project has published a best practice field guide to inform treatment and care of people with XDR-TB, established a set of principles for equitable and ethical pre-approval access/compassionate use programs, and proposed two scenarios under which compassionate use access to new drugs like quabodepistat would be deemed appropriate:

1. People with strains of TB that have resistance patterns for which an injectable agent is needed to construct an adequate four-drug regimen and in whom quabodepistat would be given in place of the injectable; and
2. People with strains of TB that have resistance patterns for which quabodepistat is needed to construct an adequate four-drug regimen.

These individuals face life-threatening gaps in treatment and exposure to 18-to-20-months of treatment with toxic medications, several of which are delivered by injection or intravenous (IV) administration requiring prolonged hospitalization. In scenario 1, quabodepistat would be given instead of an injectable or IV agent and in scenario 2, quabodepistat would be given alongside

the injectable and/or IV agent(s). Some of the individuals that meet the criteria for these scenarios may be eligible for clinical trials focused on XDR-TB that are under discussion now, however, geographic and other factors that limit clinical trial access and participation, and lengthy timelines for when such trials would be open to enrollment underscore the importance of establishing a compassionate use program in parallel to randomized controlled trials necessary to optimize treatment duration and composition for XDR-TB.

Otsuka's leadership in establishing a compassionate use program for delamanid set an important precedent and demonstrated the value of such programs for meeting the needs of individuals with limited therapeutic options and the TB programs and clinicians responsible for their care, and for generating important information necessary to support policy making, especially for the use of new drugs among populations typically excluded from formal clinical trials.[i] We urge similar action to establish a compassionate use program for quabodepistat. Results from the phase 2b/c trial presented during the 2024 Union Conference in Bali, Indonesia provides early proof of the efficacy and safety of quabodepistat, prerequisite criteria for pre-approval access to new drugs in situations of unmet medical need. The BETTER Project, Médecins Sans Frontières, and the TB CAB stand ready to support implementation of such a program, including by establishing a compassionate use protocol and medical committee to review applications, advocating with regulatory authorities, policymakers, and donors as needed, and supporting pharmacovigilance and other training. The TB CAB is also monitoring the pipeline of new TB compounds and similar correspondences are being sent out to other drug sponsors with compounds in phase II development.

By 14th May 2025, we kindly request a written response, including: (1) your reaction to the two aforementioned scenarios under which the BETTER Project and TB CAB propose compassionate use access to new drugs like quabodepistat would be deemed appropriate; (2) a detailed plan and timeline for launching quabodepistat's compassionate use program; and (3) any advocacy needs that the TB CAB can support with to accelerate pre-approval access to quabodepistat for people with XDR-TB and unmet medical need.

Sincerely,

Ani Herna Sari
Chair

Oxana Ruscineanu
Co-Chair

On behalf of the Global TB Community Advisory Board

[i] Stillo J, Frick M, Galarza J, et al. Addressing the needs of people with extensively drug-resistant TB through pre-approval access to drugs and research. Public Health Action. 2023 Dec;13(4):126-129. doi: 10.5588/pha.23.0033.