To: Ichiro Otsuka, Chairman and Representative Director
Tatsuo Higuchi, President and Representative Director, CEO
Marc Destito, Communications Director, Otsuka
Rajesh Gupta, Vice President, Global Clinical Development, Otsuka Novel Products, Tuberculosis Unit
Otsuka Holdings Co., Ltd.
2-9, Kanda Tsukasa-machi, Chiyoda-ku,
Tokyo 101-8535 Japan

Cc: Lucica Ditiu, Executive Director, Stop TB Partnership
Brenda Waning, Chief, Global Drug Facility, Stop TB Partnership
Cheri Vincent, Chief, Infectious Disease Division, USAID
Greg Perry, Executive Director, Medicines Patent Pool
Precious Matsoso, Director-General, National Department of Health, South Africa

19 September 2016

OPEN LETTER RE: Requests to improve affordability and availability of delamanid

Dear Mr. Otsuka and colleagues,

We write to you as a group of advocates, clinicians, and researchers to underscore the importance of the accessibility of delamanid (Deltyba) for treating multidrug-resistant tuberculosis (MDR-TB). As you know, delamanid is one of very few new tools we have in the armament for treating MDR-TB, and offers great hope for people with MDR-TB for whom a regimen cannot otherwise be constructed. However, programmatic uptake of delamanid remains far below what it must be to impact the MDR-TB epidemic. **We urge you to improve access by making delamanid available to all low- and middle-income countries via the Global Drug Facility (GDF) at the single, flat price of USD$54 per course and widely register the drug.**

We acknowledge and appreciate the important steps Otsuka has made to date to develop delamanid and make it more accessible, such as investing more in TB research and development (R&D) than any other private sector entity,[i] making delamanid available through the GDF to all Global Fund-eligible countries at a flat price[ii], and developing delamanid for children.

However, over two years since delamanid's conditional approval by the European Medicines Agency, and six months since its entry into the GDF catalogue, we remain troubled by the lack of availability and consequent underuse of delamanid. As of 9 August 2016, only 1,018 orders of delamanid have been placed through the GDF, including 570 from Médicins Sans Frontières; only about 350 patients are actually on delamanid. Given estimates that 30–67% of

people who develop MDR-TB each year would be eligible to receive delamanid based on World Health Organization (WHO) guidelines,[iii] this is far below the 144,000–321,600 courses needed to treat new cases alone. Several factors contribute to the low levels of uptake currently, but there are key high-impact changes Otsuka can and must make that will radically improve delamanid's availability, especially for vulnerable populations such as persons with HIV, children, and pregnant women. This is a particularly opportune time to implement these changes, as both definitive phase III trial data and WHO guidance on delamanid's use in children are anticipated in the next couple months, which we hope will support expanded use of delamanid. We urge Otsuka to:

1) **Lower the price of delamanid to $54 per course for all low- and middle-income countries.** The current lowest price of delamanid is $1700 per six-month course (approximately $233 per month), much higher than the target price of $500 for an entire MDR-TB regimen.[iv] Rigorous cost of goods modeling has shown that delamanid could be produced for just $3.50–8.60 per month.[v] We therefore ask you to lower the price of delamanid to $54 per six-month treatment course. **If you claim this is not feasible, we ask you to work with the GDF to find creative solutions to develop a realistic and still affordable counter figure or to consider voluntary licensing.** We do acknowledge that achieving low prices may require higher volumes of procurement, but without a dramatic price reduction, we are trapped in a vicious cycle where pricing prohibits the purchase of large volumes of delamanid, while the small volumes being procured perpetuate the rationale for a higher price. Otsuka could break this cycle and make delamanid more viable for widespread use by lowering delamanid's price.

2) **Expand eligibility criteria for accessing delamanid through the GDF to include all low- and middle-income countries.** The announcement of delamanid's availability through the GDF in February 2016 marked a major milestone in making the drug more easily procured, yet this was limited only to Global Fund-eligible countries. Several countries with high MDR-TB burdens are no longer Global Fund-eligible or are in transition, leaving them without a clear mechanism or price structure for procuring delamanid. The GDF plays a hugely important role in consolidating demand and streamlining procurement for TB products; providing technical assistance to countries on procurement, forecasting, and regulatory issues; and easing transaction costs, reducing administrative burden, and improving volumes and market stability for suppliers. Allowing all countries to procure delamanid through the GDF would make their procurement processes more efficient, as well as reduce effort and expense on Otsuka's end.

3) **Register delamanid in all high MDR-TB burden countries, and rapidly submit pediatric and phase III trial data to stringent regulatory authorities.** To date, Otsuka has only filed for approval delamanid in the EU, Hong Kong, Japan, South Korea, Turkey, and the Philippines, and has plans to submit dossiers in China, Indonesia, South Africa, and Vietnam. Most high MDR-TB burden countries—including Moldova and Peru, where Otsuka conducted trials leading to delamanid's approval elsewhere, and India, which

has the world's largest MDR-TB burden—remain neglected. We urge Otsuka to file for approval in these countries immediately, as well as in the U.S. as soon as phase III data are available. Furthermore, we implore Otsuka to submit updates to regulatory authorities who have already approved delamanid, including the recently available data on delamanid from children and adolescents ages 6 – 17, and as soon as they are available, the imminently expected final phase III data and pediatric data in younger age cohorts, to support expansion of delamanid's indication if warranted.

We look forward to your positive response to the above demands, which we request by 3 October 2016, and which can be directed to Wim Vandevelde at wim@eatg.org.

Respectfully submitted,
Access to Rights and Knowledge Foundation (ARK), India
DR-TB Scale-up Treatment Action Team (DR-TB STAT), Global
Global TB Community Advisory Board (TB CAB), Global
Nagaland Users' Network (NUN), India

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[iv] Médecins Sans Frontières Access Campaign. Ready, Set, Slow Down. Geneva: Médecins Sans Frontières; 2015. https://www.doctorswithoutborders.org/sites/usa/files/attachments/msf_issuebrief_drtb_readysetslowdown.pdf

[v] Gotham G et al. Target prices for novel treatments for drug-resistant tuberculosis. 15th European AIDS Conference (EACS). 21-24 October 2015. Barcelona, Spain. Oral abstract 351.