To: Mr Marc Destito
Communications Director
Global TB Program
Otsuka Pharmaceutical

24 March 2017

Dear Mr Destito,

Open letter regarding registration and availability of delamanid in South Africa

We are writing regarding the urgent need for greater availability and access to delamanid in South Africa.

World TB Day (24 March) marks a significant day for people living with tuberculosis (TB) worldwide. For South Africans, this day is particularly poignant, given that it is recognised as a high-burden country with the third highest estimated global incidence of TB (~450 000 cases per year), where nearly 300 000 people each year are notified of a TB diagnosis, including approximately 20 000 with drug-resistant TB (DR-TB)[1].

At present in South Africa, as elsewhere, DR-TB patients are subjected to taking treatment regimens with severe side effects and have to suffer through painful daily injections during their treatment. As you know, delamanid shows far fewer side effects and much improved treatment outcomes and thus could vastly improve the lives of DR-TB patients in South Africa. Delamanid has been approved for use by a stringent regulatory authority since 2014 and is registered in the European Union (conditional approval), Japan, South Korea and Hong Kong. In October 2014, the World Health Organisation (WHO) issued interim guidance for treatment of DR-TB with delamanid. However, delamanid is not registered in almost all high-burden DR-TB countries, including those where clinical trials have taken place, such as South Africa.

An estimated 7 000 DR-TB patients per year in South Africa alone could benefit from an expanded roll out of delamanid, yet less than 1% of this number are receiving access nationally. In Khayelitsha, from November 2015 until December 2016, Doctors Without Borders/Médecins Sans Frontières (MSF) supported the initiation of 55 patients on delamanid, of which 18 received it in combination with bedaquiline. Of these 18 patients, 88.9 % had a negative culture following 6 months of treatment. During the same time period, 57% of patients under 18 years old diagnosed with MDR-TB in Khayelitsha were started on an injectable-free, delamanid-containing regimen. The option to take delamanid rather than bedaquiline as part of a DR-TB regimen also allows DR-TB patients co-infected with HIV and on the standard first-line fixed-dose combination antiretroviral (ARV) to avoid switching back to multiple ARV pills.

However, the MSF cohort is the largest in South Africa, and one of the few sites offering access to the drug in the country - those who live just beyond the borders of

[1] http://www.who.int/tb/publications/global_report/gtbr2016_annex2.pdf?ua=1

Khayelitsha cease to be eligible for the MSF programme, as they cannot be regularly monitored by MSF staff. Clinicians in other parts of the country must access delamanid for their patients from Otsuka through cumbersome compassionate use procedures. Outside of South Africa the situation is not much better and, as of February 2017, fewer than 500 patients have received delamanid globally.

We acknowledge the agreement between South Africa's National Department of Health and Otsuka to provide 200 courses of delamanid for select patients through a delamanid clinical access programme (DCAP) before the product is registered locally. However, using Khayelitsha utilisation rates, we estimate that the three sentinel sites that will initiate patients through the DCAP (including Khayelitsha) will use up all of the donated courses within 6-8 months—or less, if more sites are opened.

We are gravely concerned that this short-term measure is not enough to provide sufficient or sustainable access to delamanid in South Africa. While Otsuka's engagement with the South African government is welcome, the company's efforts are already too little and too late. The above figures highlight the urgent need for action.

On World TB Day, we therefore call on Otsuka to commit to the following:

1. **To file urgently and immediately, prior to 1 May 2017, for registration of delamanid, including for children 6 years and older, with the Medicines Control Council (MCC) - either as Otsuka or through a local partner. Subsequent approval would allow the NDOH to incorporate the use of delamanid into national clinical guidelines, place it in the national Essential Medicines List, and purchase the drug through the National TB Programme.**

2. **To avoid gaps in provision of treatment prior to registration of delamanid in South Africa, we call on Otsuka to make a <u>public</u> commitment to maintain a three-month buffer stock of delamanid for additional donation to South Africa through the DCAP. Whenever the number of unused donated treatment courses falls below a threshold of 100, Otsuka should top up the donation with an additional 100 courses.**

3. **Disclose publicly which company will be responsible for local registration and supply in case Otsuka does not deal directly with the South African market, alongside any price reductions which may accompany such a distribution agreement.**

4. **Initiate negotiations with the Medicines Patent Pool (MPP) to sign a voluntary license that would enable the production of delamanid for use in low and middle income countries at an affordable price.**

The WHO has indicated a 23% improvement in cure rates of M/XDR-TB when delamanid is included in patient regimens[2]. Widespread access to delamanid is

[2] http://www.who.int/selection_medicines/committees/expert/20/applications/Memo-from-Director-GTB_27-Feb-2015.pdf

essential to bringing the DR-TB epidemic under control in South Africa. Without delamanid, people living with DR-TB in South Africa will continue to suffer. We therefore call on Otsuka to rapidly respond to our aforementioned points around delamanid availability in South Africa. Please direct all correspondence regarding this issue to Claire Waterhouse at claire.waterhouse@joburg.msf.org.

Sincerely,

Organisations:

Individuals:

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