TO: Akihiko Otsuka, Chairman
Taro Iwamoto, President
Masuhiro Yoshitake, Executive Operating Officer and TB Global Project Leader

CC: Patrizia Carlevaro, Managing Director, Otsuka SA

Otsuka Pharmaceutical Co., Ltd.
2-9, Kanda Tsukasa-machi, Chiyoda-ku,
Tokyo 101-8535, Japan

12 March 2014

Dear Otsuka leadership team,

We are writing to express our serious concerns regarding the accessibility of delamanid, an important new tool for treating multidrug-resistant TB (MDR-TB). While we congratulate you on your substantive investments in development of this drug, and appreciate your invitation to community groups to meet in Geneva, we are aware of the immediate need for this drug and ask you to commit publicly and formally to 1) immediate availability of delamanid for patients meeting criteria for compassionate use, regardless of whether they are being treated by pilot compassionate use programs; 2) rapid registration of delamanid in trial site countries and other high TB burden countries; 3) widespread availability of delamanid in TB markets post-approval, without restricting access to phase IV trials or rich countries; and 4) fair and accessible pricing of delamanid that utilizes mechanisms such as voluntary licensing, rather than tiered pricing.

1) We welcome the news that Otsuka has initiated its compassionate use program and that one patient in Europe has received delamanid outside of a clinical trial.[1] However, as requests to Otsuka to initiate compassionate use for delamanid date back to 2011, and now delamanid is poised to receive European Medicines Agency (EMA) and Japanese regulatory approval shortly, we find it unacceptable that only one patient has benefitted so far. Although there is an agreement pending for a compassionate use pilot program with Medicins Sans Frontieres (MSF), it is Otsuka's responsibility to make the drug available for patients in urgent need that meet criteria for compassionate use, and to document that use. For example, a recent case of a patient with extensively drug-resistant TB in California desperately needs more treatment options to prevent his own death, as well as to protect those around him from falling ill with an otherwise potentially incurable strain. South Africa has a very high burden of MDR-TB and urgently needs new drugs; limiting compassionate use to pilot sites prevents many patients and clinicians from accessing care to a potentially life-saving option. **Patients and providers in the many settings where pilot compassionate use programs do not exist immediately need the option to access delamanid, and to have a clear point-of-contact at Otsuka to whom to address requests. We also remind Otsuka that the risk-benefit considerations for patients in need of compassionate use access (who are by definition in urgent need of possible rather than approved treatment options) differ from those of the general population with TB, and encourage Otsuka to make delamanid available to patients hoping to benefit from the use of as yet unapproved drug combinations when no viable alternatives exist.** Of course, such

[1] http://tbonline.info/posts/2014/3/12/otsuka-response-tb-cab-crag-tag-open-letter/

compassionate use will require responsible management to ensure the drug's continued value for treating drug-resistant TB, and records of outcome should be provided to the company and in turn made publicly available.

2) To date, Otsuka has only filed for marketing approval for delamanid in Europe and Japan, with plans to file in the U.S. Claims that Otsuka will prioritize registration in trial countries are sounding increasingly hollow as the drug is poised for approval from two stringent regulatory authorities, and yet not a single filing has been initiated in a trial or other high TB burden country. **Otsuka must immediately file for marketing approval in delamanid trial site countries and other high TB and MDR-TB burden countries.**

3) We are extremely concerned that Otsuka's plans for phase IV trials post-registration are focusing on low burden settings such as Germany and the U.K. Any attempt to limit access to developed countries, whether motivated by profits or by fear of inappropriate use, are unconscionable. **Delamanid needs to be made broadly available for patients with MDR-TB worldwide, the vast majority of whom live in low- and middle-income countries.**

4) **In order to ensure this accessibility, Otsuka must affordably price delamanid.** Tiered-pricing has increasingly been shown ineffective in making drug costs accessible to low- and middle-income countries.[2] We urge Otsuka to responsibly price this drug for treating an important public health issue in all markets, utilizing mechanisms such as voluntary licensing to allow for cost-effective, quality production.

We look forward to a formal, written response addressing these concerns, as well as the availability of delamanid both pre- and post-approval for those who need it, including said patient in California. Please respond to us by March 21, 2014.

Sincerely,

Dr. Lisa Armitige, the University of Texas Health Sciences Center at Tyler (USA)
Dr. Robert Belknap, President, National Society of TB Clinicians (USA)
Prof Graham Bothamley, TBnet (UK)
Dr. David E. Griffith, the University of Texas Health Sciences Center at Tyler (USA)
Dr. Robert Horsburgh, RESIST-TB (USA and global)
Dr. Giselle Israel, Rio de Janeiro Health Department (Brazil)
Dr. Ronald Karpick, Fairfax County Health Department and Inaugural Past President, 2008, National Society of TB Clinicians (USA)
Dorothy Namutamba, Community Research Advisors Group (Uganda)
Dr. Caitlin Reed, Olive View - UCLA Medical Center (USA)
Dr. Barbara Seaworth, the University of Texas Health Sciences Center at Tyler and President Elect, National Society of TB Clinicians (USA)
Debra Shelly, Community Research Advisors Group (Global)
Lieve Vanleeuw, Treatment Action Campaign (South Africa)

[Signatories continued on next page]

[2] http://www.ip-watch.org/2013/12/10/concerns-raised-to-global-fund-over-panel-on-tiered-medicines-pricing/

AIDS-Free World (USA)
Community Research Advisors Group (Global)
Global TB Community Advisory Board (Global)
HIV i-Base (UK)
National Society of TB Controllers (USA)
National TB Controllers Association (USA)
Planeta Salud (Spain)
Securing Access to Lifesaving Treatment (SALT) (China)
Treatment Action Campaign (South Africa)
Treatment Action Group (USA)
TBnet (Europe)
TBProof (Global)