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Mr Bill Donovan
President and COO
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Dear Bill

**PROGRESS UPDATE ON THE TBDx CLINICAL TRIAL**

Drawing from the substance of our telephonic discussions, this letter serves to update you on the progress being made on the final development stages of the project and the clinical trial.

As you are aware, the technology is in the final stages of an independently controlled clinical study under the auspices of the Aurum Institute in South Africa. This study is being nested as a sub-study to another large international trial (Thibela TB Study) at the Aurum Institute which is funded by the Consortium to Respond Effectively to the AIDS and TB Epidemic (CREATE), itself funded by the Bill and Melinda Gates Foundation. The Principal Investigator for the Thibela TB Study is our CEO and world TB authority, Prof Gavin Churchyard, and he is also the senior researcher on the TBDx study. He has appointed Dr James Lewis as the Principal Investigator for the TBDx study, whilst the study includes prominent TB scientists such as Dr Gerrit Coetzee, Dr Bernard Fourie and Dr Susan Dorman amongst the paper authors.

The TBDx clinical study is governed by a protocol which has been closely designed and reviewed to ensure that it meets all international standards for diagnostic studies and has been submitted to three ethical review boards for approval. This aims to ensure that the outcomes of the study are credible at the highest levels of review and are publishable to international, peer reviewed medical literature standards. This is essential to establishing TBDx as a diagnostic tool and Signature mapping as a medical image analysis platform once the study is completed, assuming the results turn out as expected.

Performance of the TBDx system to date indicates that it performs best as an expert Decision Support System (DSS) to complement expertly trained digital microscopists, offering as additional benefits advances in productivity and lower costs of diagnosis.

Preparations for the study are progressing as planned. However a recent development change in the protocol to accommodate the DSS approach to the use of TBDx, as well as requests from end-user test experts for enhanced image analysis tools, has led to a modified protocol being submitted to the ethics committees for approval. This protocol change was implemented by the scientists to give TBDx the best opportunity to perform against routine diagnostic settings rather than just against the expert technicians who have been involved in its creation. This is a more real-world situation in which to conduct the study.

As has been extensively discussed in our weekly operations calls, preliminary results suggest that the technology may well be best placed as a 'front-end' screening technology before the use of newer but more expensive diagnostic technologies, such as the GeneXpert system from Cepheid. Given that the GeneXpert system currently costs around $20 per test, and since TBDx appears to have a high negative predictive value, TBDx may act as a low cost (approx. $5 per test) and efficient mechanism to screen out negative samples from a production run of slides, leaving only 10-20% of the original run requiring further analysis by the genetic probe system – at a substantial cost saving. The research work will test the validity of this hypothesis.

Furthermore, in settings where HIV is not as prevalent as in Africa but where the volumes of TB specimens are very high (e.g. India), TBDx in an adapted form may well be a substitute for present microscopy as well as a more cost effective alternative to GeneXpert. Again, the design of the research protocol will inform this hypothesis and suggest research work to be done for new markets.

Much has been published in the literature and in the popular press about GeneXpert. The technology is fast gaining acceptance as a very good TB diagnostic that moves diagnosis closer to the point of care. However, it is a comparatively expensive technology and has yet to be trialled on a large, operational, scale. Such trials are being planned in South Africa at present. Its deployment will require significant capital investment as well as ongoing commitments to purchase the disposable cartridges in economic volumes. In the interim, the mainstay of diagnosis remains centred on microscopy and culture techniques, and, in my opinion, any implementation of genetically based systems will have to be phased.

The crucial aspects of the TBDx study currently underway are:

- It is being conducted independently at the highest levels of scientific rigor to ensure valid results which will withstand scrutiny.
- Interest from the Principal Investigator, the Senior Scientist and other experts remains high.
- A routine high-volume laboratory demonstration project protocol has already been developed to follow on from the main scientific study should the results show TBDx performs as well as anticipated from the earlier work done.
- If successful, this will be the world's first fully automatic TB diagnostic microscopy system and will establish the underlying Signature Mapping technology as a valid platform on which to develop a host of other image based disease diagnostics.

The status of the TBDx study is:

- The London School of Hygiene of Tropical Medicine has approved the latest protocol and consequently the conduct of the research protocol has recommenced.
- The study sample size has been reduced to 1 000 slides to speed up time to results and costs of processing. There is minimal impact on the confidence intervals for the results by this reduction from the 2400 in the original study sample.
- The 1 000 slides have been re-stained and have undergone a thorough quality review against the slide inclusion criteria.
- A contract has been signed with BARC, an independent laboratory, to read all the slides twice prior to them being shipped to SMMS for processing though the TBDx system.
- The analysis system (Stata) is being programmed to receive and process the data coming back from BARC and SMMS.

The results of the study are expected to start rolling out in April 2011. In the interests of a robust and defendable outcome, it is crucial that the study follows it natural course to completion. Whilst this is a time consuming process, experience in the field of medical diagnostic development suggests that it is the best course of action to credible outcomes.

Yours sincerely

**Dr Dave Clark**
**Deputy CEO**

cc. Mr Richard Borrelli