OPTIMIZE

This is a monthly update shared with all members involved in Project Optimize, and is meant to provide a short update of major achievements, challenges, and plans for the future. Please submit any inputs to Celicia Serenata before the 1st Wednesday of every month.

Please note that some of the information in this update are confidential, so please do not share outside of OPTIMIZE.

Major Achievements from July 2016

LOW-DOSE DARUNAVIR STUDY, Wits RHI

- July saw the start of the study, with 26 patients enrolled in the study (from 60 screened) by the end of the month.
- There have been some difficulties in finding patients on 2nd line that are virologically suppressed, but the study team is actively recruiting.

ADVANCE STUDY, Wits RHI

- Wits RHI received reviewer comments from both the Wits Human Research Ethics Committee (HREC) and MCC. These comments were all reasonable, and responses were submitted on time. Final approval should be imminent.
- The 2nd version of the protocol has been shared with the Scientific Advisory Committee, ViiV, Gilead, USAID, UNITAID, and various other stakeholders. Once final comments are received, the revised protocol will be submitted to HREC and MCC (after their approvals have been received).
- Prof Francois Venter presented on the work of OPTIMIZE, and ADVANCE specifically, on several occasions during the International AIDS Conference held in Durban from 18-22 July. It was also a good opportunity to meet with consortium partners, Gilead and ViiV.

Upcoming Events

Important Contacts

Celicia Serenata, Wits RHI, cserenata@wrhi.ac.za or Skype: Celicias

Averie Gachuhi, ICAP, ab3857@cumc.columbia.edu

Jo Livermore, University of Liverpool, joanne.livermore@liverpool.ac.uk

Kellen Thomas, Mylan, Kellen.Thomas@mylan.com

NANOTECHNOLOGY, University of Liverpool

- The lead SDN candidates identified at 70 wt% loading of darunavir and darunavir/ritonavir (8:1 and 6:1 ratios) have undergone stability testing
- The radiolabelled drugs have arrived and these candidates can now be passed over to pharmacology
- Atazanavir SDNs are currently being formulated; there have been problems due to the solubility of the drug
- Liverpool now has several hits at 50% loading and work is currently being completed to check the reproducibility and to investigate increasing the loading to 60 and 70 wt% of the drug

IMPLEMENTATION SCIENCE, ICAP

- The Implementation Science (IS) concept was finalized and prepared for review.
- As part of the Y2 USAID work plan and budgeting process, it was determined that the study was not of adequate priority to warrant funding in light of budget restrictions. Work has been suspended until other resources are identified.

DEMAND CREATION AND PRODUCT INTRODUCTION, ICAP

- The Global Stakeholder Landscape Analysis has been shared with consortium partners for review.
- Case study concepts have been further developed; countries with important past transition experiences that could be shared has been reviewed with CHAI. The ICAP Kenya office collected data for the case studies. Plans have been made with USAID to introduce the case study to USAID missions.
- The Impact Overview has been shared with USAID CII for review and development of a framework to showcase country-level impact initiated.
- ICAP is coordinating with MPP to plan Y2 activities.
- Project OPTIMIZE has been introduced to the South Africa USAID mission and other key stakeholders by Wits RHI; there are plans to introduce OPTIMIZE to the USAID missions in Mozambique and Kenya – these plans are being reviewed with USAID.
- The country-level needs assessment framework has been reviewed with USAID CII; coordination has been initiated with Wits RHI to plan travel and interviews in South Africa to conduct the needs assessment.
- ICAP has started to develop a summary of all documents, reports, and meeting minutes related to market shaping.
- The ICAP staffing plan has been reviewed and revised; follow-up interviews have been held for the Market Access Officer position.

DEMAND CREATION (Community engagement) – i-Base

- i-Base published and distributed over 2000 copies of “Fit for Purpose” at AIDS2016, targeting key opinion leaders and appropriate sessions, such as “Innovations needed to support Treatment for All: From incremental to game-changing”, as well as media and community venues.[1]
- Since the May “Treatment Optimization” meeting, before the INTEREST workshop in Cameroon, AfroCAB has organized national treatment optimization meetings in Zambia, Zimbabwe, Rwanda and

[1] This project is funded by UNITAID

Swaziland. This is kicking off community demand for the new regimens and products across the continent.[2]

EFAVIRENZ 400mg TB PK STUDY, Mylan (St. Stephen's AIDS Trust)

- The Ethics Committee in London reviewed the trial at the end of July. St. Stephen's will likely need to amend the patient information sheet with the aim of obtaining approval by mid-September. The study will aim to start recruitment at the end of September (pending approval), with preliminary results expects by the end of the year, and final results before mid-2017.
- The Uganda site will not be submitted for ethics until the Ethics Committee in London approval is received. Approvals in Uganda can take up to 8 months, and thus timelines for the Uganda site are not yet defined, but ethics submission is planned for October 2016.

EFAVIRENZ 400mg PREGNANCY PK STUDY, Mylan (St. Stephen's AIDS Trust)[3]

- At the London site, 4 patients have been enrolled, with 3 patients already having completed the study. More patients are required to complete enrollment (PK required in 3rd trimester and post-partum). Final results are expected by Q1 2017.
- The Uganda site received ethics approval in July 2016. Recruitment is expected to start in September 2016, and should be complete by March 2017 (aiming to recruit 2 patients per month).

FORMULATION DEVELOPMENT (Mylan)

- TAF/FTC/DTG: Formulation development is complete. Stability initiated in Q3 2016 with pivotal bio-studies scheduled for Q4 2016. FDA submission is planned for Q1/Q2 2017, provided the bio-study results are positive.
- DRV/r/DTG: Composition optimisation and prototype developed in progress. Pilot bio-equivalence (BE) planned and Mylan applied for the licence for the BE studies. Approval for these studies is expected at the end of Q3 2016. Based on current status, the earliest filing date with the FDA is anticipated to be Q2/Q3 2017.

Major Plans for August 2016

LOW-DOSE DARUNAVIR STUDY, Wits RHI

- Introduce more recruitment strategies to meet accrual enrolment targets
- Enrol 100 participants by end of August 2016

ADVANCE, Wits RHI

- Finalise a paper on the need for ADVANCE that will be submitted to a few peer-reviewed publications
- Finalise a letter to the South African Medical Journal (SAMJ) highlighting the potential cost savings of implementing a DTG-TAF-FTC regimen in South Africa
- Brief Dr. Yogan Pillay of the National Department of Health on ADVANCE and OPTIMIZE
- Submit protocol amendment to MCC and Wits HREC

[2] This project is funded independently through AfroCAB/i-Base
[3] This study is not funded through OPTIMIZE, but is included here as a point of interest

- Issue tenders for CRO and drug procurement (for those drugs not covered by the donation)
- Confirm laboratory service provider
- Appoint Medical Officers

NANOTECHNOLOGY, University of Liverpool

- Planning the pharmacology cell lines ready for testing SDNs

IMPLEMENTATION SCIENCE, ICAP

- No further development at this point due to funding restrictions.

Staffing Changes

- ICAP is hiring a **Market Access Officer**, and a **Product Introduction Technical Advisor**

Outputs

List any articles, manuscripts submitted for review; abstracts submitted; presentations given. (Also provide electronic version of such products for the Dropbox)

- Francois Venter, 19 July 2016: Presentation at event hosted by Aspen Pharmaceuticals: "Champions rising above the challenges: Moving towards an AIDS-free generation." – Uploaded to Dropbox
- Francois Venter, 19 July 2016: Presentation at IAS 2016 session: "Innovations needed to support Treatment for All: From incremental to game-changing" – Uploaded to Dropbox