Manufacturing APIs in South Africa

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Advancing R&D of Innovative
HIV Prevention Products for Women

Introduction

- SA has a well-developed pharmaceutical formulating industry -60% of pharmaceutical products sold in SA are formulated locally.
- But 100% of APIs used to formulate ARVs and PrEP are imported.
- An estimated **60-80% of the cost of production for HIV prevention products is the API cost**.
- Currently SA imports ~$800 million worth of APIs annually, mainly from India and China.
- Local manufacture of APIs for HIV prevention will
  - secure the supply chain
  - improve the speed and efficiency to introduce new treatments
  - significantly reduce costs
  - allow for expansion of current HIV prevention programs

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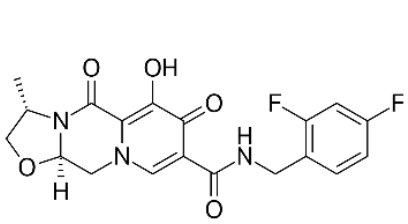
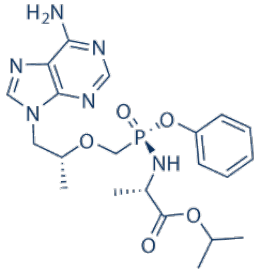
Project Aims and Objectives

12-month Independent Special Project has three objectives:

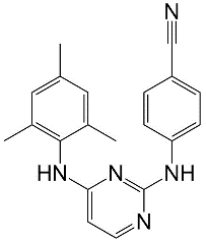
1. *Cost competitive* process optimizations for the synthesis of up to three different antiretroviral agents;



cabotegravir



tenofovir alafenamide



dapivirine

2. *Technology transfer* of cost-effective flow reactor "Synthetron" systems from USA to SA
3. Establishing a process chemistry *skills development hub* in SA

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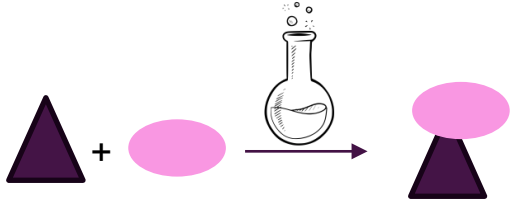
Unique Partnership Model

The H3D Foundation is a non-profit organization that was established in 2019 to complement the work of the H3D Drug Discovery and Development Centre's capacity building programs. H3D Foundation aims to position Africa as a global player in innovative pharmaceutical R&D by building infrastructure as well as the skills of scientists and researchers based in Africa.

H3D Foundation developed the project proposal, brought together the team and is managing the project.

commercialization.

Flow vs Batch Processes



Batch process requires complete mixing of reagents for a fixed period, followed by isolation and purification (Current industry norm)

- Large production facility required –capital intensive
- Scale up requires careful research and the yield is not linear
- Larger volumes introduce inefficient mixing
- Less control at scale -greater safety risks
- Batch variation

Flow reactors require a steady flow of reagents through the reactor and produce a steady supply of product.

- Low set up cost
- Smaller lab footprint
- Easy scale up (scaling is linear)
- Greater control -inherently safer
- Faster mixing -efficient heat transfer
- Cleaner product, less waste
- High reproducibility

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Synthetron Flow Reactor Technology

- Small lab footprint (1 x 2 meter)
- Very small reaction volumes (0.25 mL)
- Highly efficient (producing multi-kilogram quantities < 1 hour)
- Accommodates a wide range of reaction conditions
- Higher concentration (cheaper than batch)
- More efficient chemistry resulting in higher yields
- Greater reaction control
- Spinning disk reactor creates a dynamic mixing environment for greater efficiency

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Progress

- Legal agreements in place
- Team in place, including hiring of three fellows
- Reactor manufacturing initiated
- Paper chemistry and design of preferred synthetic routes and optimization points identified
- Ongoing input from CPT Pharma on commercial considerations (costing, availability of reagents, solvents suitable for scale up, other potential issues)

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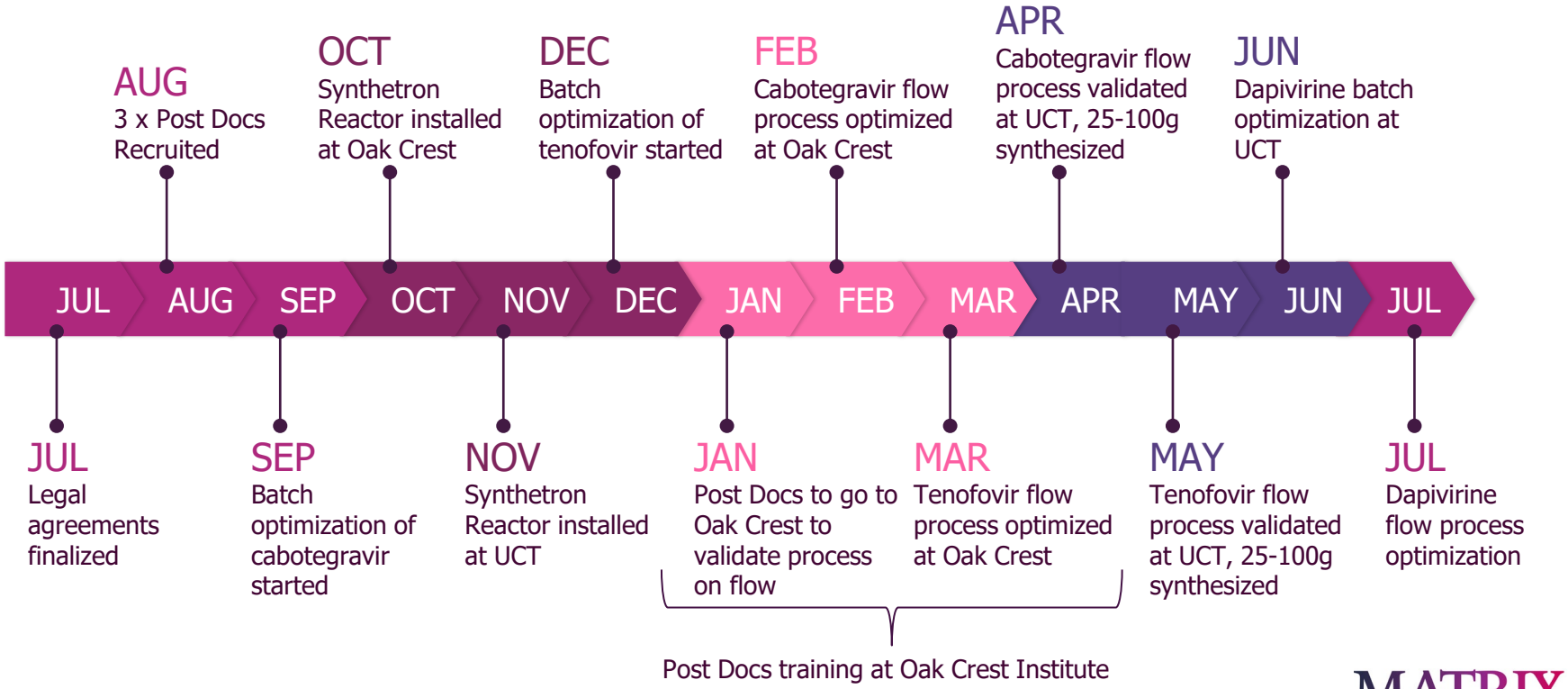
Timeline 2023-2024



Acknowledgements

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