

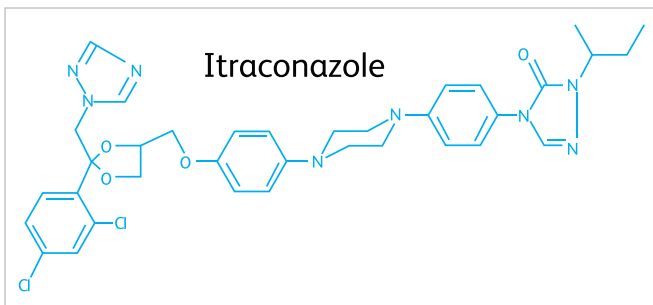


## FACTSHEET

### Proof of Concept Study

#### Service Offering

- Aptuit INDiGO™ is a service which provides fast access to human data even for poorly bioavailable drugs.
- The deliverables include Phase I clinical trial supplies and regulatory (IND/CTA) documentation in as little as 26 weeks when API is supplied. API production can also be included in a 52 week option.
- Services cover API manufacturing, toxicology, metabolism/ pharmacokinetics, clinical supplies and regulatory application.
- Various formulation approaches are available. One unique approach is the use of an amorphous dispersion in a capsule (ADIC). This dosage form provides improved bioavailability for poorly soluble compounds without formulation development and provides an easy administration route for first-in-human clinical trials.



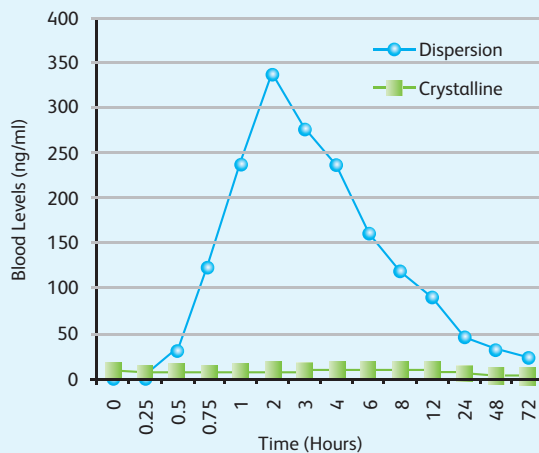
#### Proof of Concept Study

- An internal proof of concept study was conducted at Aptuit using itraconazole as a model compound.
- Itraconazole is a very poorly soluble weak base with an aqueous solubility estimated at approximately 1 ng/ml at neutral pH and approximately 4 µg/ml at pH 1. The calculated log P is 6.2 and is classified as a class II drug in the Biopharmaceutical Classification System.
- The project started with an amorphous dispersion screen to find a suitable dispersion. Five polymers at four concentrations were tested.
- A 1:2 itraconazole:HPMC-P (hydroxypropylmethyl cellulose

phthalate) dispersion was chosen based on characterization, scale-up, physical stability, and limited performance assessment.

- For a feasibility batch, the dispersion was scaled up to over 200g using a spray drying subcontractor.
- The material was tested and encapsulated, packaged in foil pouches, and put on stability.
- For clinical trial manufacture, over 700g of dispersion was produced by spray drying, tested, encapsulated, and packaged under cGMP conditions; the material was then put on stability.
- Information was added to the IND template as work progressed to keep to the timeline. The IND was completed on time. The stability testing is in progress.

#### Comparison of Blood Levels



#### Results

- An animal bioavailability study in dogs was performed to compare the 1:2 itraconazole:HPMC-P dispersion in a capsule to the itraconazole crystalline material in a capsule.
- A significant increase with the dispersion was observed which confirmed our limited performance assessment.



## FACTSHEET

### Proof of Concept Study... cont'd

#### Timeline

The timeline below summarizes key milestones of the project. Material was received on May 17 and the project completion date was November 15.

#### Additional Aptuit Capabilities

Aptuit offers a comprehensive array of services and a proven track record in API, preformulation, formulation, method development, analytical chemistry, physicochemical analysis, stability testing,

technology transfer, manufacturing, clinical packaging and distribution across a wide range of compounds, dosage forms and delivery systems.

For information about Aptuit's services, please call or email:

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**Engineering a better drug development process.**

