



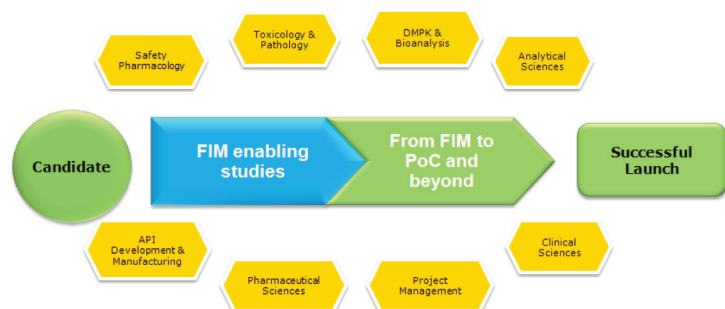
From FIM to PoC and Beyond

Overview

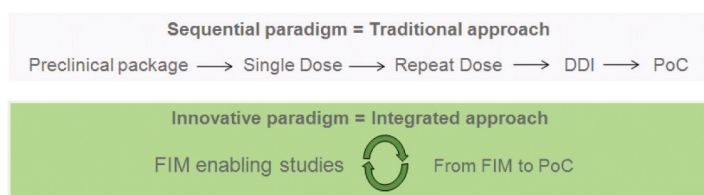
The challenge of the development in new drugs from candidate selection to launch resides in the high clinical attrition rate. In fact, only 8% of new drugs will successfully make it up to launch and the attrition rate for new molecules entering clinical development is on average 85%. The probability of success for compounds in Phase I & II has a significant impact on overall development costs, in a way that clinical development accounts for approximately 60% of the cost for each new drug.

Benefits of Integrated Drug Development at Aptuit

Our integrated drug development approach has been designed to facilitate the close interaction of highly experienced disciplines at the cutting edge in understanding the causes of attrition and applying the most advanced approaches to reduce it. The earliest establishment of efficacy, acceptable safety and PK profile in human leads to an efficient and rapid decision-making process.



Aptuit offers integrated drug discovery and development solutions beginning from target validation through to clinical proof of concept studies and beyond.



Additional benefits associated with an integrated approach include effective team-work and shorter cycle times during the iterative stages of drug development due to co-localization of all contributing disciplines and a project manager as the driver.

The following disciplines support stand alone or integrated services for FIM to PoC and beyond:

- Drug Metabolism and Pharmacokinetics Bioanalysis
- API Development & Manufacturing
- Pharmaceutical Sciences
- Toxicology and Pathology
- Safety Pharmacology
- Clinical Sciences
- Analytical Sciences
- Project Management

The benefits to clients are evident through the rapid cycling of information between pre-clinical and clinical studies in a way that clinical development issues are identified and addressed as soon as possible. Aptuit's portfolio of the tools allowing early establishment of efficacy and safety profile includes:

DMPK

- *Ex vivo* metabolite identification and quantification in biological matrices of pre-clinical species
- Assessment of systemic exposure data in pre-clinical species during long-term tox studies
- Early evaluation of major human circulating metabolites and assessment of toxicological cover (MIST, Metabolite In Safety Testing)
- Definitive identification and quantification of human metabolites
- Disproportionate circulating metabolites ADME characterization
- Assessment of metabolic and transporter mediated DDI potential through *in vitro* and *in vivo* studies. IVIVE (In Vitro In Vivo Extrapolation) to guide DDI clinical strategy and co-meds inclusion/exclusion criteria
- Investigative pre-clinical studies to assess the distribution, accumulation and potential retention of a new drug (parent compound and metabolites)



From FIM to PoC and Beyond

Bioanalysis

- Clinical Bioanalysis support including Dried Blood Spot
- *Ex vivo* protein binding determination in special patients population

API Development & Manufacturing

- Drug substance manufacturing and release in a GMP environment
- Synthetic process definition, optimization and scale-up including transfer to manufacturing sites
- Integrated approach to form and version selection, optimization and control
- Solid State and Physical Properties handling
- Iterative process for the formulation optimization *via* design and improvement of the API physical properties
- Quality by Design approach to regulatory filing *via* identification of API control strategy

Pharmaceutical Sciences

- Assessment of the available dosage form (API formulation & processes) *vs.* target product profile (TPP) as for PK/PD relationship
- Formulation development and *in vitro* support to the set up of clinical studies for biopharmaceutics understanding of dosage form performance
- Drug delivery system refinement and optimization (i.e. formulation and delivery route) driven by clinical data de-convolution and statistical analysis
- Quality by Design approach to regulatory filing for Drug Product e.g. Identification of CQAs and CPPs to design product quality and consistency against its required clinical performance
- Scalability and manufacturability assessment

Toxicology and Pathology

- Pre-clinical investigative and problem-solving studies: customized, fit-for-purpose, integrated assessment of multiple endpoints
- Regulatory general toxicology studies

Safety Pharmacology

- Pre-clinical investigative and problem solving studies: customized, fit-for-purpose, integrated assessment of cardiovascular and central nervous system
- Regulatory Safety Pharmacology studies
- Consultation and conduction of abuse liability studies

Clinical Sciences

- Design and implementation of clinical plans
- Design, conduct, analysis and interpretation of healthy subjects and patient studies
- Translational and Experimental Medicine
- Medical governance
- Due diligence and in-licensing support
- End-to-end study operational leadership
- High statistical and PK competence for planning, executing and reporting both standard and innovative clinical trials
- Advanced statistical methodologies (i.e. Bayesian approach)
- Population PK & PK/PD modeling

Analytical Sciences

- Integrated analytical control strategy to guide the clinical product delivery process from synthetic route development to manufacturing of pharmaceuticals
- Complex chemistry, chiral and mass balance issues, in-process controls and pilot plant support to manufacturing
- Complete packages of analytical services for new drug development in a GMP environment
- Analytical services customized for each phase from early definitions to analytical Tech Transfer, applying the principles of Quality by Design
- LIMS in place to ensure a great deal of control and GMP/GLP compliance of all analytical activities



Aptuit Verona

FACTSHEET



From FIM to PoC and Beyond

Project Management

All of these activities are carried out under the supervision of a dedicated project manager, with the aim to deliver quality services agreed with the client on time, in full and always ensuring a high scientific standard.

Conclusions

The Aptuit integrated drug development approach gives clients the opportunity to work with a single service provider for their drug development needs with seamless transition from one stage to the next with evident associated benefits of attrition reduction and timeline compression.

Additional Aptuit Capabilities

Aptuit offers a comprehensive suite of drug development services that range from drug discovery through to market, including consultancy services, API development and manufacture, preclinical technologies, clinical sciences, pharmaceutical development services, large and small scale manufacturing, IVRS and clinical packaging and logistics, 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 through scientific excellence.