The Aptuit Center for Drug Discovery & Development – Verona, Italy

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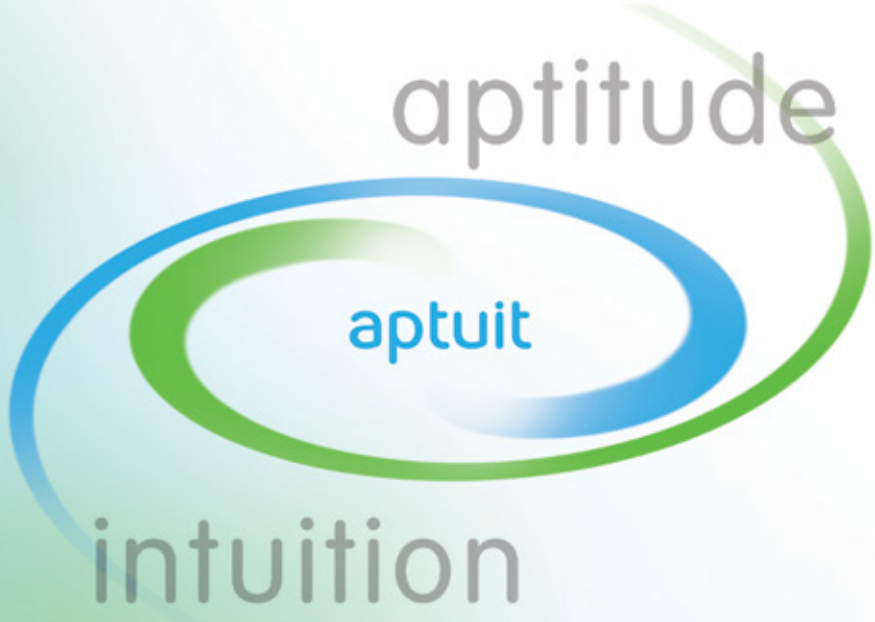
Aptuit in Verona: uncommon expertise, exceptional results

A knowledgeable scientific group, comprised of some of the industry's foremost drug discovery and development experts, forms a collaborative team at The Aptuit Center for Drug Discovery & Development in Verona, Italy. They are specialists with uncommon expertise in neuroscience, antibacterial, oncology, cardiovascular, respiratory and other key therapeutic areas. Together, with our other development sites in the US and the UK, these experts stand among Aptuit's vast, global assembly of talented people.

Essential throughout the development process is the Project Manager who serves as the client's advocate and ensures exceptional results. Focused on the fastest, most efficient and lowest risk option, Aptuit's Project Managers are highly experienced professionals who fully understand that the client and Aptuit are most effective when working together in a partnership that is flexible, trustworthy and transparent.



The Best of Both Worlds: a CDDO and an R&D Engine

The Aptuit facilities in Verona, Italy, combine the proven efficiency of a Contract Drug Development Organization (CDDO) with the established scientific expertise of an accomplished and successful Research and Development engine. When compared to typical contract providers, it is significant that the experience of much of the scientific staff has been attained *within* the pharmaceutical industry, rather than simply *for* the pharmaceutical industry.

Scientists at the facilities have advanced a large number of molecules from early discovery through clinical development with low attrition rates on many target classes. Their expertise in multiple therapeutic areas imparts a strong measure of confidence and credibility for pharmaceutical clients. Working as a highly integrated team, Aptuit scientists take a solution-driven approach, progressing compounds efficiently, expeditiously and economically.

GMP authorization for both API and drug manufacturing and testing facilities are in place with regulatory inspections performed by AIFA, the Italian Drug Agency, and the FDA. Preclinical facilities for biological studies are fully GLP certified by the Italian Ministry of Health according to OECD principles. GCP compliance has also been determined for testing of human samples and management of clinical studies.

Integrated Knowledge: a unique, dynamic differentiator

Integrated Knowledge captures all that is exceptional about The Aptuit Center for Drug Discovery & Development. The term stands for the essence of what clients – whether they represent large, multinational companies or emerging biotechs – can anticipate as a unique, reliable and consistent advantage when they select Aptuit as their partner.

Specifically, Integrated Knowledge represents layer upon layer of the insights and understanding of a collaborative group of multidisciplinary scientific experts and their support teams who routinely have access to the most advanced technologies. The Integrated Knowledge of scientific professionals in Drug Design & Discovery, Preclinical Biosciences, Pharmaceutical Sciences and Clinical Strategy is a significant and dynamic Aptuit differentiator. Integrated Knowledge is the driving force in taking the client's molecule through to finished drug product with maximum efficiency.

What distinguishes **APTUIT**

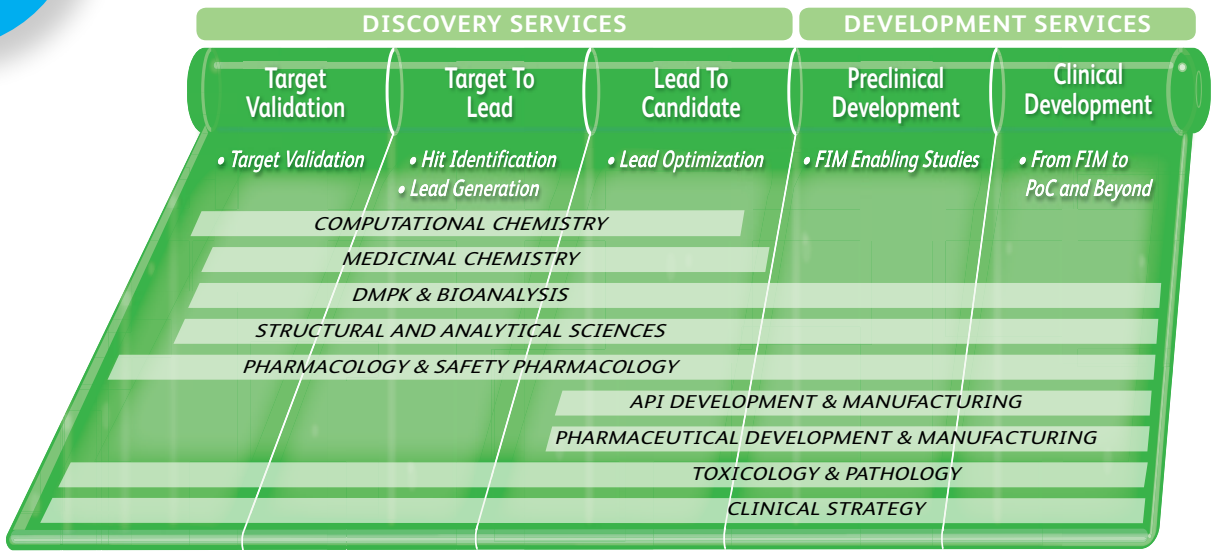
INTEGRATED KNOWLEDGE
Layers of shared insights and understanding of multidisciplinary experts

Benefits for both integrated and stand alone services

Whether clients choose an Integrated Service Offering or select stand alone services, they experience the Integrated Knowledge of scientists at The Aptuit Center for Drug Discovery & Development, who share an insatiable quest for learning and are able to grasp all the subtleties and implications of the entire picture. Their all-encompassing vision of the process, always in the spirit of sharing their individual knowledge with each other, allows for a deeper, greater understanding of the parameters set forth by the client. Significantly, the broadened perspective of Integrated Knowledge allows for the identification of challenges that may surface later on in the process. Therefore, as the process unfolds, Integrated Knowledge mitigates risks by anticipating potential problems and suggesting preemptive solutions.

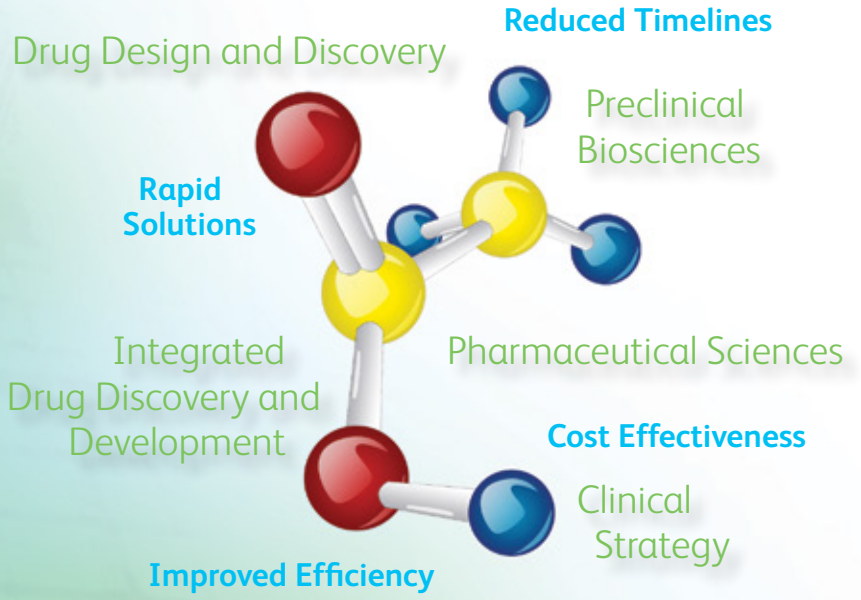
Seeing the whole picture, anticipating potential problems, suggesting preemptive solutions

The Aptuit Integrated Service Offering



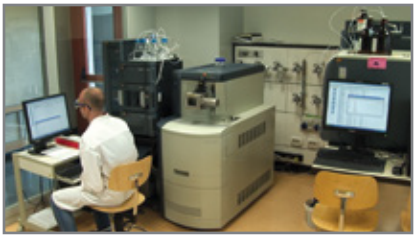
Fully integrated services from a single site

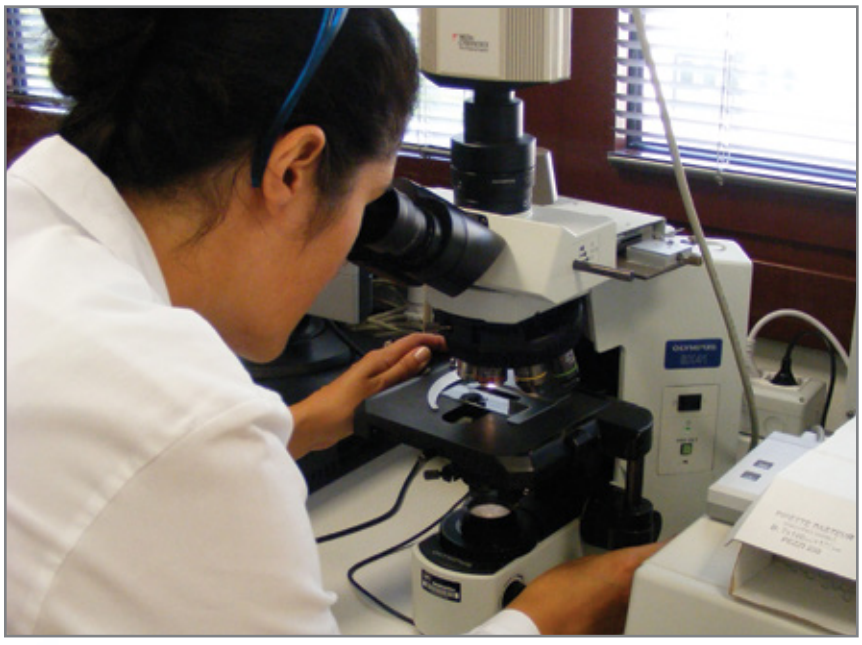
The facility's broad range of integrated capabilities includes Drug Design and Discovery, Preclinical Biosciences, Pharmaceutical Sciences, Clinical Strategy and Integrated Drug Discovery and Development programs. For clients, fully integrated drug discovery and development services from a single site deliver a number of tangible benefits such as reduced timelines, cost effectiveness, elimination of technical or informational transfers and efficiency to provide rapid solutions. Successful processes are in place to advance the client's molecule from discovery to finished product.



Experts in overcoming early development challenges

The breadth of Aptuit's capabilities in Verona bring added value to clients who are accustomed to dealing with several suppliers. Clients experience convenience, time and cost savings, and an exceptional level of quality performance that is the result of well established collaborative expertise.
Among the other notable capabilities available from The Aptuit Center for Drug Discovery & Development are Integrated Non-Human Primate Facilities and Applied Immunology services. A full range of exploratory/ preliminary, regulatory, investigative, customized and fit for purpose studies can be conducted. AAALAC accredited animal facilities and procedures are used. In addition, preclinical development studies of vaccine/viral vector/gene therapy, such as GLP biodistribution and virus shedding, are available.





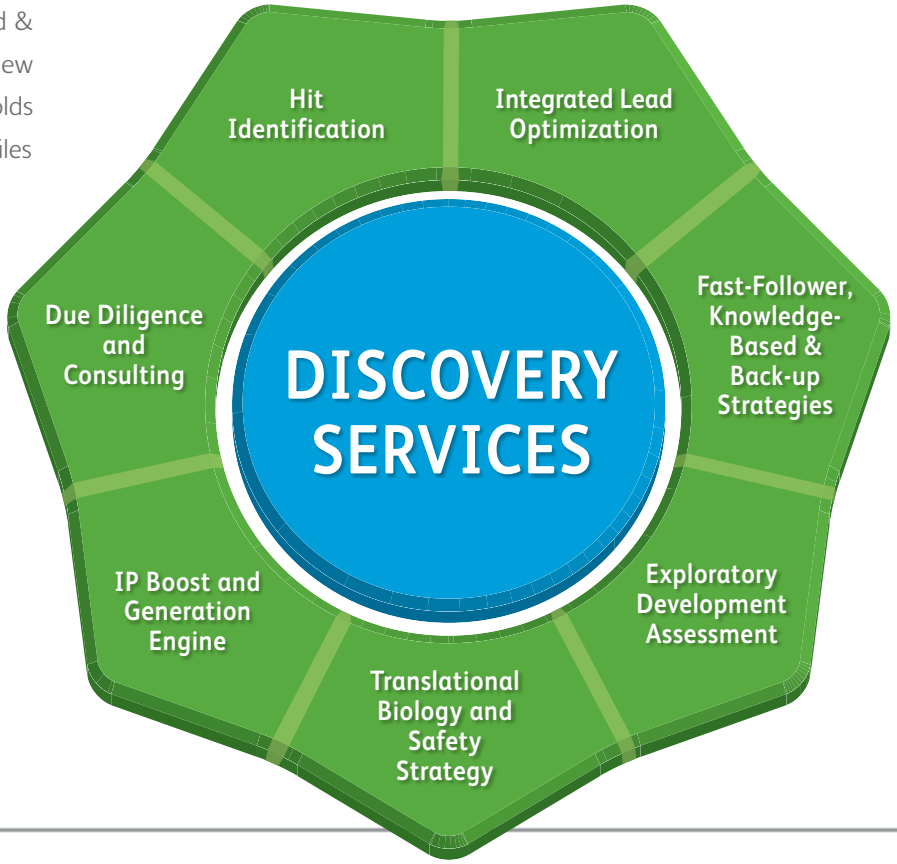
Drug Design & Discovery from Target to Lead to Candidate

Aptuit's comprehensive Drug Design & Discovery processes are led by scientists with experience in target identification and validation of preclinical candidate molecules. Core discovery services, available as a fully integrated offering or as stand alone services, include: Computational Chemistry, Medicinal Chemistry, Discovery Biology, Pharmacology, Drug Metabolism and Pharmacokinetics (DMPK), Safety Assessment, and Analytical Discovery Support. In addition, expertise in Toxicology, Pharmaceutical Sciences and Clinical Strategy capabilities are brought into the process for a truly translational approach.

Aptuit can provide Drug Design & Discovery solutions exceeding those normally associated with CDDO offerings, providing a versatile range of value-added business options best suited to individual client needs. Among these unique options are bundled Drug Design & Discovery and Preclinical Biosciences services. The bundled Aptuit offering of these services from a single site delivers integrated capabilities of the highest quality at substantial cost savings.

A comprehensive range of Drug Discovery capabilities

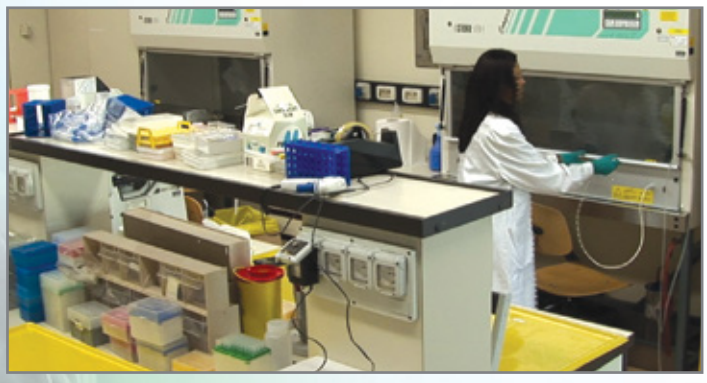
- Hit Identification: featuring UHit, Aptuit's comprehensive, alternative approach that employs Virtual HTS computational screening through 2D/3D descriptors and structure-based ligand-based *de novo* design, and Discovery Biology, targeting activity and selectivity screens (affinity and/or functional in recombinant cell lines or native tissue)
- Integrated Lead Optimization: an advanced approach that relies on fully integrated research units, multi-factorial optimization and a Fit-for-Purpose strategy
- Fast-Follower, Knowledge-Based & Back-up Strategies: innovating new chemistry for existing drugs/scaffolds to improve safety and efficacy profiles
- Exploratory Development Assessment: including preliminary Safety and DMPK when there is a low quantity or poor quality of available API
- Translational Biology and Safety Strategy: "Bench to Bedside" research that expedites the translation of scientific discoveries into clinical practice
- IP Boost and Generation Engine
- Due Diligence and Consulting



Preclinical Biosciences, taking a customized approach

The Preclinical Biosciences team at The Aptuit Center for Drug Discovery & Development can perform the full spectrum of preclinical studies, with the assurance of accurate and balanced assessments even when meeting the tightest deadlines. Scientists employ best-in-class technologies to find the solutions that suit client's requirements. From laboratories within the Verona site, they share their expertise in Microbiology, Pharmacology and Safety Pharmacology, Toxicology & Pathology, Drug Metabolism & Pharmacokinetics and Preclinical and Clinical Bioanalysis. The integrated Aptuit team is distinguished by specialized preclinical capabilities. A legacy of success in applied immunology services and in conducting studies for biotherapeutics are notable.

Preclinical Biosciences offers expertise in CNS disease, antibacterials, substance abuse, oncology, cardiovascular and other key therapeutic areas.

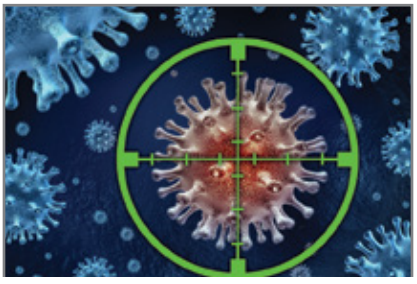


Experienced in the preclinical development of GTMPs

The Preclinical Biosciences group is comprised of molecular and cellular biologists, immunologists and toxicology/pathology experts who are dedicated to projects related to the development of Gene Therapy Medicinal Products (GTMPs). The team can perform GLP studies for GTMPs that include integrated parallel toxicology/pathology, efficacy and biodistribution studies, with flexible study plans to accelerate preclinical development.

Before the release of the GTMP, quality tests on produced batches are performed, including: titer determination, pseudotyping identity (for viral vectors), residual DNA contamination, stability studies and transgene identity.

A key component of GTMP development is quality control testing, including:



Titer determination

Stability studies

Pseudotyping identity (for viral vectors)

Transgene identity

Residual DNA contamination

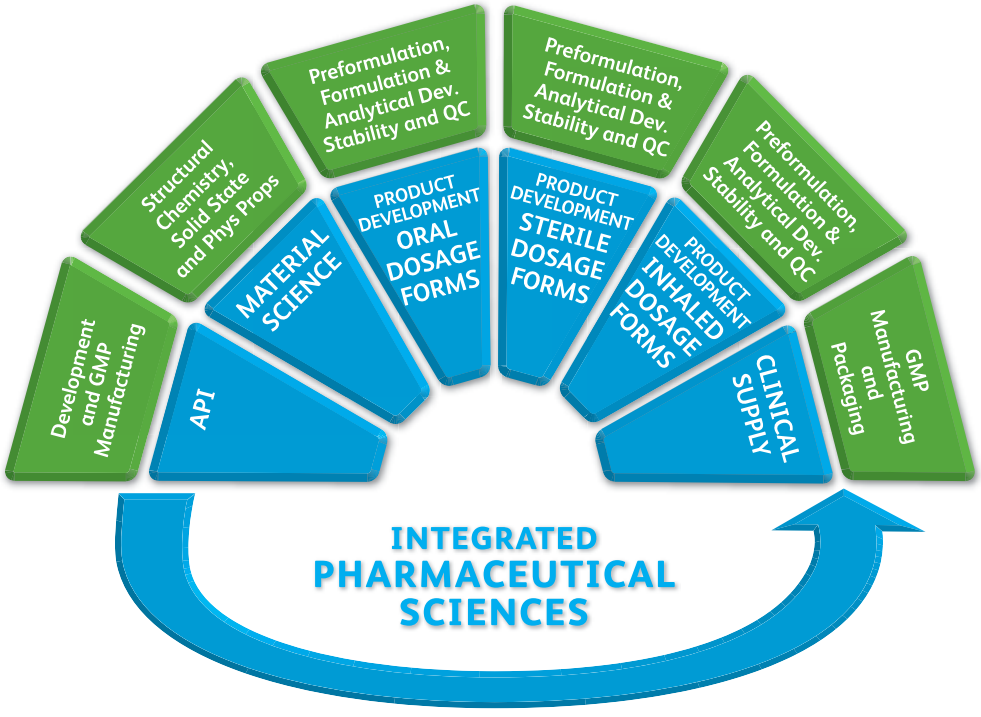
Pharmaceutical Sciences, all under one roof in Verona

Aptuit clients can rely on fully integrated Pharmaceutical Sciences services from the Verona site. Well established capabilities in Chemical Development and Manufacturing, Pharmaceutical Development, Analytical and Physical Science and Clinical Supply conjoin to make Aptuit the ideal Pharmaceutical Sciences partner. The seamless integration of drug substance and drug product services, all performed under one roof in Verona, provides clients with a distinctive advantage: every aspect of their project is accomplished by a single, unified, collaborative team.

Aptuit's Pharmaceutical Sciences team takes "the big picture" approach in the development of both drug substance (API) and drug product. The broadened perspective of Integrated Knowledge enables scientists to address early findings that foresee potential issues that might surface later on in the process, avoiding or mitigating the risks of unexpected delays and costs.

Complementary Vision, a novel way to deliver services

Aptuit has initiated a new way of delivering Pharmaceutical Sciences, known as "Complementary Vision." This harmonized approach encompasses all of the services that precede and follow the Pharmaceutical Sciences profile. Cost efficiency and time saving benefits through the design of the dosage form that best fits the preclinical/clinical needs are the result of this novel approach. Pharmaceutical Sciences clients can rely on a combination of *in silico, in vitro* and *in vivo* services. The results substantiate the design, development and selection of the most effective dosage form for the intended clinical use, throughout the application of biopharmaceutics from early to late development stages. A comprehensive review process is undertaken for generic drugs to meet up-to-date regulatory requirements. Expertise in API development and manufacturing ensures the timely delivery of the required quality of API to support both toxicological and clinical studies. Aptuit also provides the required analytical support, including method development and validation and batch release. Lean Six Sigma business processes are in place, helping to ensure total quality management.



Aptuit INDiGO,® addressing today's challenges

A significant solution to overcoming the time and cost challenges of drug development is Aptuit INDiGO.® This accelerated development process uses integrated, parallel development tracks to advance API to regulatory submission in as few as 26 weeks. In just 52 weeks, compounds can progress from candidate selection to regulatory submission, a highly desirable alternative to the industry average of 122 weeks. By adding 30 additional weeks, Aptuit INDiGO® takes the compound into the clinical phase and provides human safety, tolerability and pharmacokinetics results from First In Man studies. To date, Aptuit's multidisciplinary teams of experts have successfully implemented more than 60 Aptuit INDiGO® packages across a wide range of therapeutic areas for small and large molecules, drug product changes, and post FIM and IP extension opportunities.

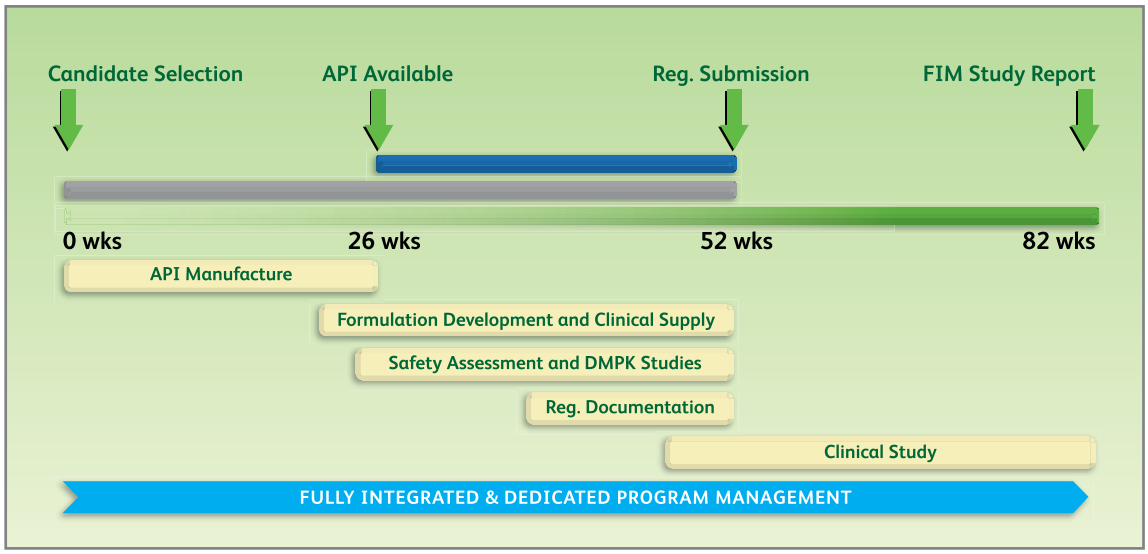
Aptuit INDiGO® can be customized to advance your molecule from candidate selection to FIM/POC studies

- World class preclinical safety/DMPK & solid state chemistry
- \+ Quality-by-design principles applied in earliest stages
- \+ Seamless data and knowledge integration throughout project
- \+ Regulatory documentation preparation & Clinical Sciences
- \+ Reduced service provider monitoring
- = aptuit INDiGO®

Accelerated development, real time data

When performed at The Aptuit Center for Drug Discovery & Development and other global sites, Aptuit INDiGO® addresses other industry challenges by providing an integrated approach. The accelerated process overcomes the negative effects of dealing with multiple outsourcing companies or incurring difficulties created by inefficient handoff between multidisciplinary groups. Aptuit INDiGO® also delivers a real time, high quality data package with interpretation in key development areas, not something that is commonly found when clients are working with other contract providers.

Optimized timelines are achieved by using integrated, parallel development tracks



Industry average based on Tufts CSDD analysis: 122 weeks (Compared with Aptuit INDiGO® 52 week package)

- **As few as 26 weeks from API availability to Regulatory Submission**
- **As few as 52 weeks from Candidate Selection to Regulatory Submission**
- **Only 30 additional weeks from Regulatory Submission to FIM study report**

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The Aptuit Center for
Drug Discovery & Development
– Verona, Italy

Via Alessandro Fleming 4
37135 Verona (VR)
Italy

+39 045 8218111

For information about Aptuit's services, please contact us:

in Europe: +39 045 821 9333
in the US: 855-506-6360

email us at: expertise@aptuit.com
www.aptuit.com

Aptuit's Global Family of World Class Facilities

Aptuit Corporate Headquarters, Greenwich, Connecticut

West Lafayette, Indiana

Aptuit SSCI is recognized around the world for its solid state chemistry leadership.

Glasgow, Scotland

Aptuit's Glasgow, Scotland site is known for its sterile fill finish and formulation development.

Oxford, England

Aptuit's API facilities in Oxford, England, feature strong competencies in API development and manufacture.