

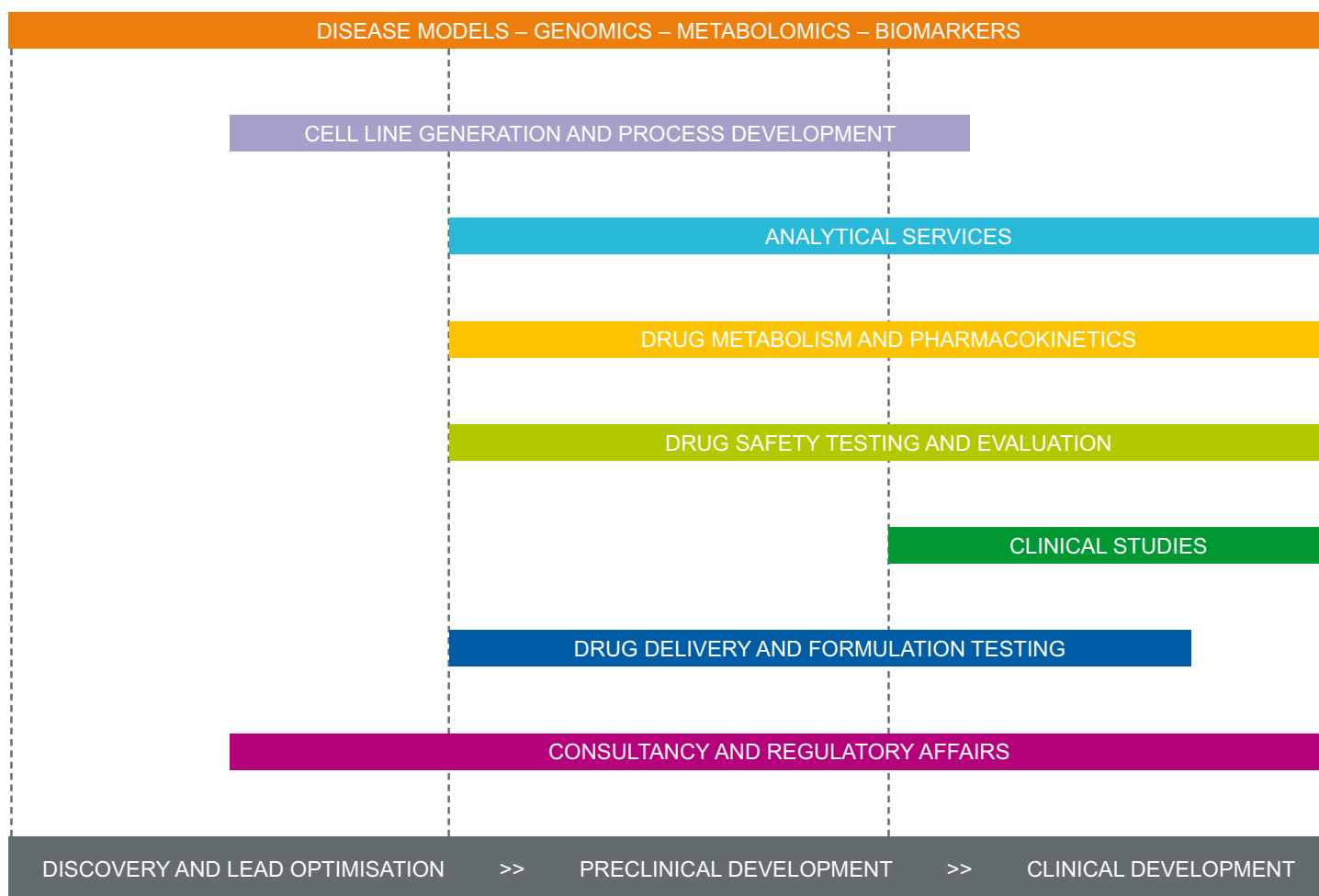
TNO Pharma services: from discovery to the clinic

TNO | Knowledge for business



Preclinical drug development is facing the triple challenge of becoming quicker, more cost effective and more predictive. As the single organization offering both strategic advice and comprehensive laboratory services in bioprocess development, product characterization, safety and efficacy, TNO helps its clients rise to meet these challenges.

What are your goals in drug development? How may we assist you?



Cell line generation and process development

TNO applies a range of vectors, expression systems and culturing technologies. This allows you to pick the best option to develop a scalable process with an optimal speed, yield, purity and regulatory profile. For instance, we can apply a parallel strategy for cell line generation using multiple platforms. By using transient transfected cell pools, a small batch of a biopharmaceutical candidate can be produced at a very early stage. This enables you to reach milestones earlier and to check for critical aspects at an early stage (e.g. fate of compound in the body, proof of concept). At TNO, there is a close link between cell line generation and process development and safety and efficacy assessment. This raises the odds of having a process that can be transferred to a GMP facility in the shortest possible way, while managing CMC costs.

Analytical services

Our analytical sciences professionals offer standard, as well as highly innovative, techniques and services. These services include developing bioanalytical models using state-of-the-art equipment and analyses. With our experienced team and extensive range of analytical instrumentation, we can devise solutions to analyze and characterize biopharmaceutical and small molecule drug candidates, to assess immunogenicity and to measure biomarkers in complex matrices. Process development of biopharmaceuticals is enhanced by novel monitoring and data processing techniques. Increasingly, gene expression patterns and metabolomes are used to improve productivity or to enhance safety and efficacy assessment.

Drug metabolism and pharmacokinetics

Our kinetics & metabolism experts can help you select and further develop your

candidate drugs with a comprehensive preclinical pharmacokinetic toolset. Our services range from early absorption and metabolism screening systems to predictions of human kinetics. Our expertise includes monoclonal antibodies, enzymes, vaccines, hormones, peptides and other proteinaceous materials, as well as nucleotides, cytokines, lipids, carbohydrates and small molecules. In cooperation with our pharmacology experts, we can also generate DMPK data in disease models.

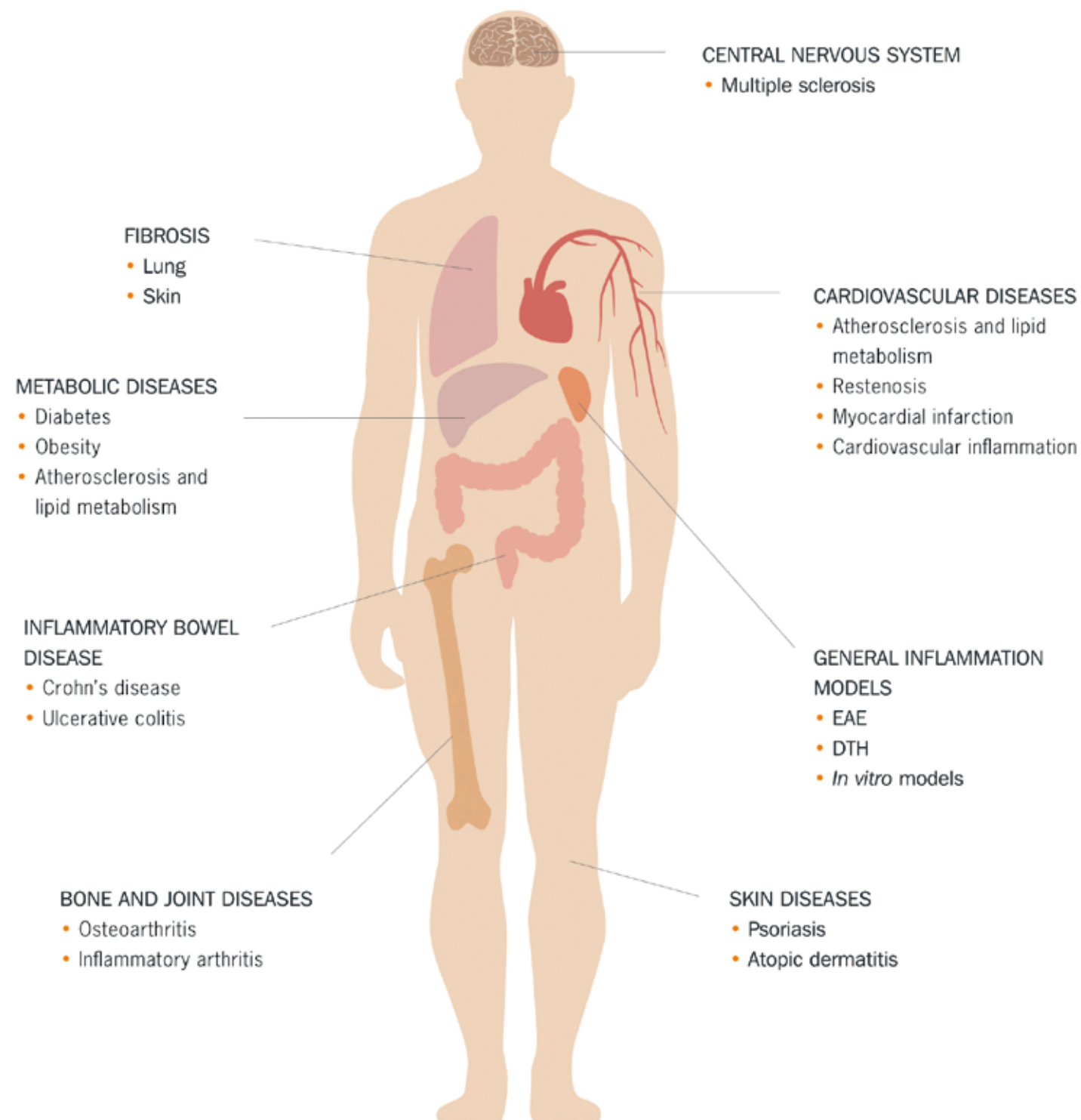
Disease models and efficacy

Representative disease models are very useful in obtaining important information in the following areas:

- Efficacy
- Compound prioritization
- Target identification
- Target validation
- Mechanism of action

Disease expertise and models

Portfolios of validated *in vivo* and *in vitro* disease models are available in the following areas of expertise:



In years of research, we have gained a wealth of knowledge about a number of disease areas and disease processes. This expertise is supported by a large portfolio of well validated *in vitro* and *in vivo* models, a range of often unique read-out parameters and an extensive academic and clinical network.

Drug safety evaluation

From small molecules to biopharmaceuticals, TNO will perform your studies promptly, reliably and in accordance with the latest guidelines. We have a strong reputation in toxicological research and compound safety evaluation. Toxicology and safety

pharmacology studies can be performed at TNO using any relevant route of administration. Areas of specialization include the GI tract, the respiratory tract (including aerosol generation and monitoring technology), the immune system and the nervous system.

Drug delivery and formulation testing

TNO offers you a full range of drug delivery testing services for new formulations and drug delivery systems. We investigate bioaccessibility and bioavailability via various administration routes, using *in vivo*, as well as *in vitro* techniques, including TNO's famous patented *in vitro* models of the GI-tract, TIM. In the area of formulation development, we specialize in polysaccharide-based matrices for proteins, peptides and small molecules with site-specific or on-demand release characteristics.

Clinical studies

Your clinical trials require medical expertise and reliable project management. Our clinical trial unit is equipped with its own dedicated team of physicians, project managers, research nurses, dieticians and technical and administrative staff. All these professionals work in accordance with the ICH guidelines and GCP. In the last

two decades, our experts have completed numerous pharmacokinetic, bioavailability, safety and efficacy studies. These were dermal absorption, penetration, inhalation and/or nutritional studies and include first into man single, ascending, repeated dose and drug-drug, drug-food interactions.

Consultancy and regulatory affairs

In product development it is essential to consider the relevant country-specific and internationally harmonized guidelines that could affect the product. Our knowledge of the most recent legislation makes it possible for TNO to assist clients in key matters concerning international regulatory procedures for new pharmaceutical products. Furthermore, TNO offers multidisciplinary consultancy and project management services, including quick scans, test strategy development, project planning, feasibility studies, expert opinions and independent reviews by a trusted third party.

TNO Quality of Life

TNO Quality of Life is a part of TNO; Europe's largest independent research institute for technological and strategic research and consultancy. By translating scientific knowledge into practice we optimise the innovative abilities of the industry and government. As a research partner TNO works for various industries worldwide.

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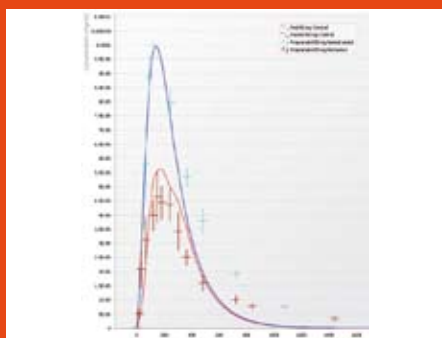
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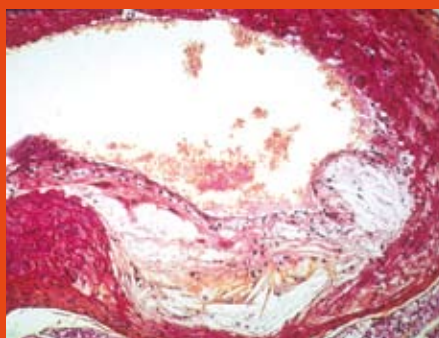
TIM, *in vitro* gastrointestinal model



Biacore T100



PK: *fasted and fed state plasma levels*



Atherosclerosis in E3L transgenic mice