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SKULDTECH

**SKULDTECH EXPERTISE IN
INNOVATIVE MOLECULAR
DIAGNOSTIC DEVELOPMENT**



I. Company overview

Skuldtech is a French biotechnology company specialized in the discovery and the validation of new biomarkers for diagnostic and therapeutic purposes.

The company uses its expertise in-house for developing new genomic and pharmacogenomic diagnostic tests.

To achieve these goals, the company has established an advanced platform using new high-throughput sequencing (NGS) technologies and proprietary tools.

In particular, Skuldtech possesses a bioinformatic and biostatistical platform capable of processing and analyzing millions of pieces of data generated by high-throughput sequencing. The company leverages over 12 years acquiring expertise examining and interpreting this type of data.

Skuldtech business model is based on two main business lines:

- Services for discovering genomic and pharmacogenomic biomarkers dedicated to research and diagnosis applications, as well as for helping to develop new drugs. The company gives its clients and partners the benefit of its experience and technologies by offering a range of services that are adapted to the needs and issues at stake for a given project.
- In-house innovative diagnostic development for personalized medicine applications.

II. Skuldtech expertise in molecular diagnostic development

Skuldtech has acquired a strong background of expertise alongside innovative molecular diagnostic development pipeline.

A. *Biomarker discovery process*

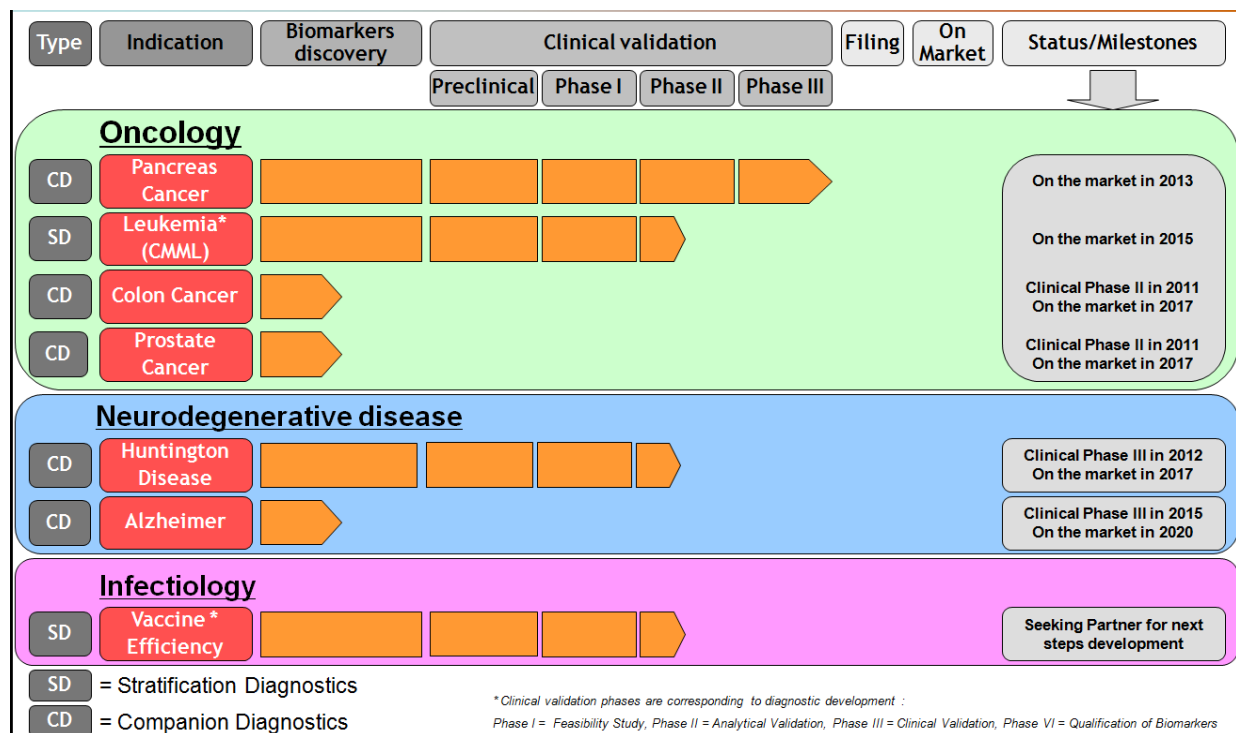
During the course of its R&D and service activities, Skuldtech has identified dozens of genomic markers in correlation with disease prognosis, drug efficiency, and early detection of pathologies (See following panel of biomarkers discovered by Skuldtech). These markers were identified in different types of tissues, organs, and for specific biological questions (such as pathologies, drug effects, etc.).

Skuldtech developed its technology platform for RNA and DNA analysis based on high-throughput sequencing techniques, such as Roche/454 Life Science and Illumina 1G sequencer, Applied SOLID[®], and more. These analysis technologies are able to identify and quantify extremely specific nucleic acids, that is carrying out exhaustive and objective analyses of all nucleic acids present in the cell. In particular, this includes all types of coding RNA (mRNA) and non-coding RNA (small RNA, pseudogenes, etc).

In order to process and analyze the millions of pieces of data generated by high-throughput sequencers, Skuldtech uses its proprietary bioinformatic tools and database, as well as biostatistical tools specifically developed for studying the data in question, and designed for the integrated analysis of biological information. This approach optimizes interpretation and ensures that it makes biological sense.

B. Molecular diagnostic pipeline

Skuldtech develops in-house innovative molecular diagnostics dedicated to personalized medicine. For instance, the company is involved in clinical trials for developing diagnostics (companion diagnostics) associated with new therapies. Within this business line, Skuldtech has developed a strong expertise in clinical trials for diagnostic validation and a pipeline of molecular diagnostics (See following figure).



C. Molecular diagnostic design know-how

After the biomarkers identification stage through NGS platform, Skuldtech selects biomarkers for routine diagnostic kit through Real-Time PCR (RT-PCR) technology. The company designs 96 well plates with specific primers for a multiple devices (Roche, Applied...) use. Thus, Skuldtech has developed a sound background in designing RT-PCR 96 well-plates for production and manufacturing issues. Skuldtech provides RT-PCR 96 well plates through manufacturing collaboration. A complete in-house assembly line is planned to be operational at the end of 2012.

Skuldtech has also developed an expertise in designing primers associated with innovative biomarkers and setting-up protocols dedicated to service provider diagnostic laboratories. Some of Skuldtech primers and protocols are currently in use within service provider laboratories, especially in the field of animal health.

D. Clinical pharmacogenomic services

Skuldtech has extensive experience in clinical pharmacogenomics. The goal of these analyses is to facilitate evaluation of clinical pharmacological parameters such as:

- Dose response
- Treatment efficacy
- Safety - Toxicity - adverse effects

It also enables optimization of clinical trial design.

Skuldtech has established expertise and tools that enable it to meet new FDA guidelines (Guidance for Industry: Clinical Pharmacology: Premarketing Evaluation in Early Phase Clinical Studies - February 2011) in an accurate and effective manner, while serving the needs of pharmaceutical and biotechnology companies with respect to clinical pharmacogenomics.

- **Over 12 years experience in pharmacogenomics:** For over twelve years, Skuldtech has been developing tools and processes, and consolidating its expertise in identifying genomic biomarkers for research and diagnosis applications, as well as for helping to develop new drugs.
- **Recognized by leaders in the field:** Skuldtech collaborated with Roche Diagnostics on the first analysis of transcriptome data on the Roche/454 Life Sciences Sequencer System and on elaborating experimental protocols with Solexa.
- **Expertise in clinical pharmacology:** Skuldtech benefits from significant experience in pharmacological development for clinical trials. The company is currently in Phase III clinical trials for an oncology application; Phase II for an application for neurodegenerative disease with diagnoses associated with therapies (companion diagnostics); and in the clinical phase (study phase demonstrating clinical benefits) for a disease progression diagnosis/prognosis in oncology.
- **Cutting-edge bioinformatics tools:** Skuldtech leverages its proprietary bioinformatics platform, which can process millions of pieces of data obtained from next-generation high-throughput sequencing (NGS). This unique bioinformatics platform interprets data and integrates it into all types of bioinformatics databases.
- **Biostatistical data integration:** Skuldtech integrates all of its pharmacogenomic analyses into a specific biostatistical platform that integrates tools that were specifically designed to analyze genomic data as well as more traditional models. These biostatistical approaches also cover both experimental schemas and specific interpretation of biological NGS data.

III. Skuldtech biomarker panel

A. Biomarkers associated with therapies/drugs

Skuldtech has discovered several biomarkers able to identify the responder patient versus the non responder one leading to determine therapy/drug efficacy.

- Biomarkers for pancreatic cancer efficacy (**currently in phase III clinical trials**, project granted by French financing organism),
- Biomarkers for Huntington disease treatment efficacy (**currently in phase II clinical trials**, project granted by French financing organism),
- Biomarker associated with Erythropoietin (EPO) drug abuse (project granted by USADA, AMA, AFLD),
- ...

B. Biomarkers associated with disease detection, evolution and prognosis

Skuldtech has identified biomarkers able to detect disease at early stage and monitor the disease evolution, supporting the physician decision for treatment prescription.

- Biomarkers for stratifying patients with chronic myelomonocytic leukemia in order to adapt treatments appropriately (**currently in phase II clinical trials**),
- Biomarkers for monitoring Huntington disease evolution (**currently in phase II clinical trials**, project granted by French financing organism),
- Biomarkers for early detecting, monitoring and managing animals with osteochondrosis disease,
- ...

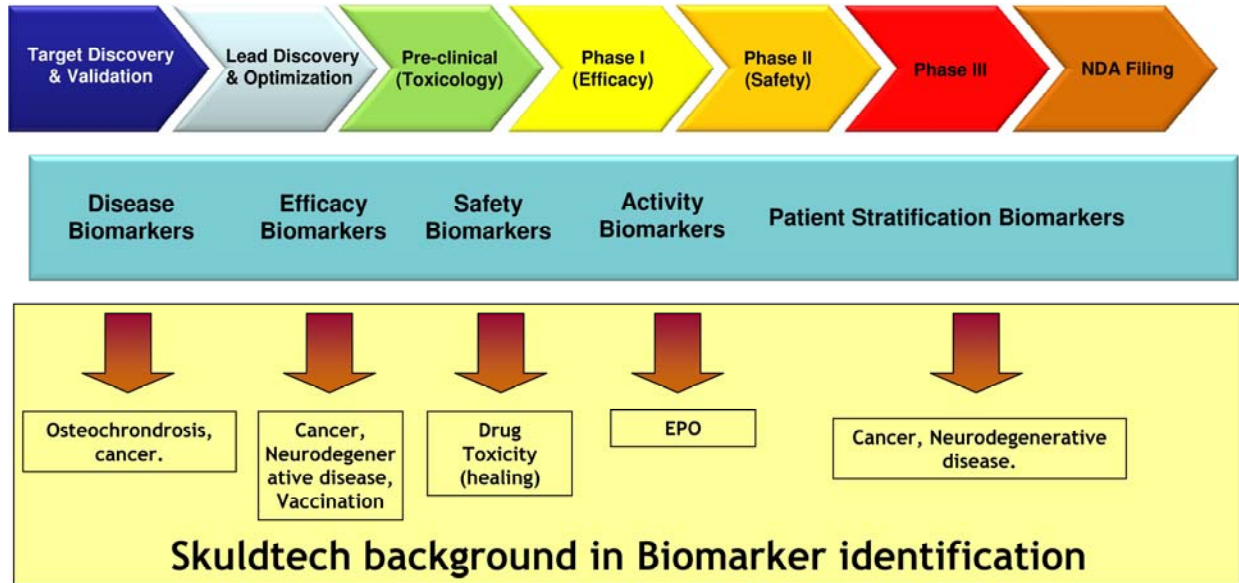
C. Biomarkers associated with immune response, vaccination and infectious diseases

Through its service business as well as in its in-house developments, Skuldtech has identified and validated a panel of biomarkers associated with:

- Efficacy in dog vaccination protocol against Leishmania, Rubarth's disease, Canine Distemper and Rabies (French Ministry of Health granted project),
- Host pathogen interaction in Leishmania infection (EU granted project),
- Resistance of Leishmania infection in human and mouses (EU granted project),
- Resistance of trypanosimia infection (calf),
- Detection of pathogens: Dengue (EU granted project), Hantavirus (EU granted project), Leishmania (AIEA granted project)...
- ...

D. Biomarkers associated with pharmacogenomics

Skuldtech has developed expertise at every step of the drug discovery process



IV. Bibliography relative to Skuldtech

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