… Senior industry experts advising young Biopharma Companies
And the Investor Community…

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Who are we?

We are a team of Biopharma Industry experts with medical and scientific training and qualification. Each of us has more than 30 years of industry careers including senior management and executive functions.

Our experience spans from basic research in Chemistry, Biochemistry and Immunology over Clinical Development, Regulatory Affairs, Development Drug Safety and Pharmacovigilance including Risk Management, Medical Affairs and Quality Assurance (GxP). With our expertise we provide integrated or focused strategic and operational advice and support to our clients. These include Biopharma Industry, Trade Associations, Governmental Bodies and Investors.

What do we offer?

We offer expert advice and operational support for

- Drug Development and Regulatory Strategy and Planning
- Focused Development and Regulatory advice tailored to the needs of young and start-up companies, including design and organization of Proof-of-Concept studies
- Preparation and conduct of Agency Meetings (FDA, EMA, national Competent Authorities)
- Process definition, organizational design and implementation of post approval Drug Safety Risk Management
- Design and implementation of Development Risk Management process
- Organizational and managerial advice for infrastructure development
- Due Diligence assessment
- Feasibility and risk assessment of drug development projects targeted to Investors and Analysts

Our Professionals have extensive experience in drug development. They offer the accumulated and integrated expertise of more than 30 years each, of personal participation in, and leadership of, drug development programs in small, mid-sized and big Pharma.
They see their mission in advising young and start-up companies on the most efficient drug development approaches, combining in depth real life development know-how, regulatory, drug safety and GxP knowledge and experience.
Innovative, time and cost efficient development designs are applied in the framework of regulatory guidelines, evaluating drug and indication specific opportunities within the spirit and intent of regulatory requirements and expectations.

The primary objective is to support the drug development, including proof-of concept studies, with the most time and cost efficient program resulting in data standing regulatory and due diligence scrutiny.

Specialized Services

- *Drug Development strategy and planning*
- *Regulatory strategy, including orphan drug applications*
- *Support for meetings with Regulatory Agencies in Europe and US*
- *Development of Proof-of-Concept studies*
- *Advise on selection of clinical investigators and CROs*
- *Advice and support for Drug safety management, including Risk management*
- *Meetings with potential licensees and/or Investors*

Drug Development Strategy and Planning

Drug development, and more specifically clinical development, is a very resource intensive activity within a biopharma company. This is not only due to the high costs for performing clinical trials and especially in Phase III (therapeutic confirmatory) but also to the high failure rate in drug development as a consequence of demonstrating efficacy and safety.

A development strategy, tailored to the characteristics and potential of the drug is key to time and cost efficiency within the NPV (maximized Net Present Value) objective. Minimization or avoidance of non-productive cash burn and loss of time to valid results are factors which companies are striving for. Development complexity seen with traditional NCEs (New Chemical Entities) becomes even more challenging for innovative drugs and especially new therapeutic approaches such as Advanced Therapies due to their nature and their higher intrinsic risk for failure.

A drug development strategy should be mainly data driven without ignoring the vision of the drug's potential. Translation of a scientific idea and vision into a realistic drug development strategy based upon hard data and experience can limit the risks for failure and optimize the “bench to bed” process. It also allows for early prioritization between potential indications or products in the development portfolio.

“Pharmakon experts have the experience of a sizable number of drug developments and have designed innovative drug development strategies.”

The value of a good drug development strategy is only determined by its success through transformation of the strategy into a corresponding smart and slim development plan. Definition of the therapeutic indication, clinical trial endpoints, patient inclusion/exclusion criteria, time lines, milestones, and management of trial conduct are decisive for success or failure.

“Pharmakon experts have experience in numerous clinical trials and the assessment of the adequacy of clinical trial protocol designs.”

Regulatory Strategy

The final aim of all drug development efforts is the regulatory acceptability of the data created through the development process and the subsequent Marketing Authorisation. A regulatory strategy that underlies and supports the development plan provides a solid foundation to all development efforts.

The regulatory strategy should intelligently and creatively be driven by the properties and potential of the developmental drug/therapy. In order to optimize the regulatory acceptability of a specifically tailored drug development program, it needs to take into account the spirit and intent of regulatory guidelines, principles and expectations.

Consideration should be given to various regulatory options like orphan drug status, scientific advice, special protocol assessments and other available interactions with, and support from, regulators for selecting the most time and cost effective alternatives.
Early inclusion of regulators in the scientific rationale of development choices can drive the regulatory strategy and drug development plan. Such approach can avoid unnecessary/non-suitable pre-clinical studies and clinical trials which would not adequately address the thinking and potential concerns of regulators.

"Pharmakon experts have longstanding and proven expertise and experience in regulatory strategies and interactions with regulators. "

Meetings with Regulatory Agencies in Europe and US

Although meetings with Regulatory Agencies are an excellent opportunity to receive advice and feedback on specific items of discussion, they can also be a source of misunderstandings and misinterpretations on both sides of the table. This can result in divergent or wrong understanding of agreements and expectations raised by both parties, leading to decisions with negative time and cost impact.
A meeting with a Regulatory Agency should result in unequivocal, valid conclusions.

In order to drive meetings to success, thorough and detailed preparation is indispensable. Meeting time is usually limited so that it is mandatory to optimize presentations so that all issues can be addressed and clarified.
The content and quality of the briefing document and the preparation of the company experts for the meeting are key determinants for the quality and usefulness of the outcome.

Regulators usually do not pro-actively exploit all regulatory options. At a stage of limited data availability, they tend to lean more to conservative approaches driven by basic concerns and perceived limitations
In order to achieve tangible, optimized results, well prepared company representatives should lead and inspire regulators, through conclusive scientific reasoning, to think out-of-the-box and buy in, if necessary.
Meeting rehearsals with internal and external experts have proven to be a very good basis for a successful meeting.

Scientific Advice and other regulatory meetings with EU Regulatory authorities,

In the European regulatory system these meetings with regulatory authorities and their representatives were introduced to support, early on in development, pharma companies in their development efforts for achieving at the end a Marketing Authorisation. Specifically with innovative drugs and new therapeutic approaches, the Authorities see the need to be early involved in the understanding, assessment and co-development of the scientific rationale. This helps them to create and shape their own thinking and approaches for future data evaluation and benefit risk considerations.

Who (EMA, national Competent Authorities, ...) to meet and when is dependent on various factors like strategic and tactical regulatory objectives, chosen/compulsory regulatory procedures, scientific expertise and experience of a specific national Competent Authority, stage of development, etc.

Pre-IND, End-of-Phase II and Pre-NDA/BLA

FDA has a long tradition of meetings with companies. Most known, and key for optimizing regulatory strategy and development plan are the Pre-IND meeting prior to filing an IND and starting the first clinical trial, the End-of Phase II meeting to discuss and agree the Phase III clinical trials, and the Pre-NDA/Pre-BLA meeting to discuss and agree on the completeness and the details of the presentation of the contents of the NDA/BLA. Various other meetings can be requested if justified by valid reasons, e.g. unexpected data in order to agree on how to address and design appropriate changes to the original development program.

"Pharmakon experts have prepared and conducted numerous meetings with EMA/CHMP and FDA. Specific expertise has been built for the preparation of company and external experts including the conduct of rehearsals"

Proof-of-Concept/Principle Studies (PoC/PoP)

A Proof-of-Concept/Principle (PoC/PoP) study is a major milestone in a drug development. It is not only the decision point for major resource investments but it is also the first time that the scientific idea on which the development is based, will be expressed in terms of human clinical data.
In the context of raising additional capital or building partnership with other companies, the PoC/PoP trial is the key step in the development of the drug candidate. It will allow increasing considerably the value of the drug candidate and the young biopharma company for a relative modest investment.

Therefore, the design and conduct of a PoC/PoP study is crucial in order to establish appropriate data with the most added information value at lowest costs in the shortest period of time.

The primary purpose of a PoC/PoP study is to demonstrate the validity of the underlying scientific rationale for a drug candidate/therapy in patients suffering from the targeted disease or volunteers within a disease model.

Optimization of a study design should be achieved through an appropriate definition of the therapeutic indication and patient/model selection criteria. It is the aim to show the drug effect(s) in the smallest number of patients/volunteers. This should be done based on thorough assessment of all available data and information rather than future market vision and expectations.

Within a carefully selected and focused indication, patient/volunteer selection criteria, treatment modalities, concomitant treatments, patient visit schedules/assessment time points and selection of adequate endpoints are determining components for a successful study protocol.

Since the purpose of PoC/PoP studies is the first demonstration of a clinical effect of a drug candidate the endpoint(s) should demonstrate that the underlying scientific rationale is translated into the postulated effect in a defined clinical situation. Therefore, in a PoC/PoP setting, trial endpoints don't necessarily need to be the same as regulatory endpoints in pivotal (Phase III/Therapeutic Confirmatory) trials.
For PoC/PoP studies, frequently surrogate endpoints are acceptable. The selection of the clinical or surrogate endpoint is decisive for the final value of the PoC/PoP study

"Pharmakon consultants designed and performed various successful PoC/PoP protocols and studies"

Selection of Clinical Investigators and CROs

Selection of clinical investigators is very often a difficult balance exercise between investigational skills and experience, patient recruitment potential and Key Opinion Leader importance.

For PoC/PoP trials, focus very often is on a specific methodology/technical infrastructure and pre-experience in the type of protocol or other non standard requirements which are important for the feasibility and success of the trial.

For later phase clinical trials clinical which require higher number of patients, clinical trial experience and patient recruitment potential are more important.

CRO selection and contracting should be based on a thorough assessment of the CRO's capabilities, stability of staff and fit with the company's way of managing service providers. Since in most clinical trials the major part of the trial budget is spent for CRO services, it is important to make the right choice in order to have a clinical trial conducted and completed in time, at the right quality and within budget.

"Pharmakon consultants have extensive experience and substantial expertise in investigator and CRO selection and management."

Drug Safety Management

Drug Safety and Pharmacovigilance have come into the focus of attention not only of Regulatory Agencies but also of the public. Legal requirements in Europe (Clinical Trial Directive, Volume 9a) and legislation in the US (FDAAA) have put the bar for safety management higher and higher. Also during the drug development phase attention is moving more and more from reactive safety information reporting (Individual Case Safety Reports (ICSR), Annual (Safety) Reports) to pro-active safety risk management.

If in the past the *benefit* over risk was determining drug approval. The tendency now is that *risk* over benefit is becoming decisive. Appropriate drug safety management from the very beginning of a drug development can be decisive for good decision making throughout development and the approvability of an effective drug.

Risk Management Plans

A Risk Management Plan (RMP)/Risk Evaluation and Minimization Strategy (REMS) is a documented commitment of a company how to manage identified and potential risks as well as to minimize the risks after the Marketing Authorisation has been granted or a NDA/BLA is approved. In the EU a RMP is compulsory for any new Marketing Authorisation Application (MAA) while in the US FDA has to determine for each NDA/BLA whether a REMS is required. In both regions RMPs and REMS have to be submitted together with the MAA or NDA/BLA, respectively.

Under-assessment of identified and potential risks and/or under-commitment of risk minimization actions can substantially delay a Positive Opinion of the CHMP or the approval of the NDA/BLA. On the other hand, over-assessments and over-commitments can put an undue burden on the company as post-approval commitments. A well designed and well performed process for the creation of a RMP/REMS will rationally and reliably result in appropriate RMPs/REMSs.

"Pharmakon experts have in-depth experience and expertise to assess, design and support implementation of Drug Safety processes and procedures as well as thorough experience and expertise in process design and procedural implementation of RMPs/REMSs"

Meetings with Potential Licensees

Licensing (out) is an important and complex process and decisions are mainly driven by scientific assessments of the drug (candidate), usually through a thorough due diligence process involving subject matter experts. The licensor should be able to display the drug (candidate) as a desirable object for the licensee to acquire.

Basic information in the confidential data package must provide to the potential licensor a comprehensive understanding of the drug's capabilities (established data), its intrinsic potential (extrapolated data), and its possible limitations in order to support credibly the expected market potential. All of this should be data driven and needs to carry the licensor's vision of the drug as well as to display his scientific and business competence. Despite the need for disclosing at this point of the process all relevant data and information for the assessment by the potential licensee, the protection of Intellectual Property must be guaranteed.

For building the Data Room usually a specialized law firm will support the licensor to assure that all information is provided in the accessible documents which is necessary to avoid later claims of the licensee. However, company scientists have to work with the lawyer(s) to avoid and to take appropriate measures that no unprotected or potential intellectual property is disclosed.

Company experts should be prepared (and potentially rehearsed) to discuss questions raised in the Due Diligence sticking to facts and figures and support the agreed objectives and vision for the drug.

"Pharmakon consultants have gone through various Due Diligences and established substantial experience and expertise in the preparation and the conduct of meetings with potential licensees"

Services provided through the Pharmakon Network of Senior Consultants

In addition, by longstanding professional relationships with other senior bio-pharma industry experts, Pharmakon has established a network providing expertise and experience in complementary Biopharma industry disciplines.

- *Pre-clinical development : toxicology, safety pharmacology and ADME*
- *Warehousing and distribution of experimental medicines and European QP release*
- *Advice on manufacturing and packaging of experimental medicines*
- *Bio-Statistics and Data Management consulting and operations*
- *Pharmaco-economics, Pricing and Reimbursement*
- *Medical Writing*
- *GCP and cGMP auditing*

Monique PODOOR, M.D.
President, Pharmakon S.A., Luxemburg

Monique is the founder of Pharmakon S.A., a consulting company providing strategic and operational advice, including due diligence, to Bio-pharma Industry, Trade Associations, Governmental Bodies and Investors.

Monique has been in pharmaceutical industry since 1977 and worked in both clinical research as well as regulatory affairs in positions of increasing responsibility to executive functions in several companies, among them Schering A.G., Beecham Pharma, Cyanamid International, Hoechst, Bristol-Myers Squibb, Schering Plough, and Janssen. Throughout her career she worked on a number of different developmental and marketed drugs, among others cytostatic drugs in breast cancer, hematological oncology, hormone therapy in prostate cancer, hormones for infertility and for contraception, anti-virals in HIV and hepatitis, antibiotics, cytokines, anxiolytics, antidepressants, antipsychotics, anti-Parkinson drugs, melatonin agonist, cardiovascular drugs, vaso-active drugs, gastro-intestinal drugs, topical corticosteroids, antihistamines, anti-hirsutism drugs, X-ray contrast media etc.

As a consultant Monique has been supporting the development and the subsequent filing of several new products through the different registration systems in Europe. She has acted as the key contact person with EMEA on several occasions.
She has been managing till November 2007 the operations of the EORTC, a pan-European academic research organization in cancer.

Monique is acting as a consultant to Trade Associations and Health Authorities on the implementation of the EU Clinical Trial Directive and specific clinical research topics. She is a regular lecturer at the University of Brussels and on several international platforms and the co-author of the reference manual “Clinical Trials in Belgium”.

Gerd JOHNSCHER, Ph.D.
Senior Consultant, Pharmakon S.A., Luxemburg

In January 2008 Gerd joined Pharmakon S.A. as Senior Consultant. Prior to this he was with UCB S.A., Belgium. There he was for 5 years Head of CNS Development where he developed Keppra, a blockbuster anti-epileptic drug. Gerd created and managed over 7 years a global Regulatory Affairs organization which performed UCB's first and successful FDA NDA and EMEA centralized submissions and approvals as well as the first Mutual Recognition procedure. He built and headed for 10 years global, integrated Drug Safety (development and pharmacovigilance) and Quality Assurance (GxP) organizations. He also developed drug safety Risk Management processes and procedures. In parallel he managed for 7 years Global Medical Affairs and for 3 years HS&E. He also conducted various due diligence assessments for acquisitions of licenses and companies. His last position with UCB was Senior VP, Advisor to the CEO. He was also Board Member of various companies.

Prior to joining UCB, Gerd spent more than 2 years with G. H. Besselaer Assoc. (now Covance) in charge of Business Development Europe, including regulatory and development consulting for US biotech and Japanese companies.

He started his industry career with Hoechst AG, Germany working for 5 years in Biochemical Research about T-cell immunology and lymphokines (2 patents) as well as carbohydrate chemistry, which resulted in an assignment by Pharma Production for the transfer of a manufacturing process from Canada to Germany. He built the basis for his development and regulatory career during 8 years in International Clinical Research and Regulatory Affairs with the responsibility for Northern Europe and North America. He finally spent 2 years in the Strategic Planning Group of the Pharmaceutical Division in charge of international development and regulatory strategies.