EDITORIAL: Striving for the High-Hanging Fruits

Drug discovery is operating in an environment that is becoming even more challenging. Apart from increasing regulatory hurdles, the reimbursement of a drug, which is crucial for success in the market, will depend on its breakthrough innovation potential, i.e. providing significant difference in the care for patients and convincing scientists, regulatory authorities, insurance companies, physicians and first and foremost the patients.

At the other end of the value chain, in the early stage of drug discovery the situation is changing towards a significantly increasing ratio of targets associated with an inherently poor chemical tractability. This does not only include targets with a low probability to bind small molecules such as those involving protein-protein interactions but also targets associated with highly demanding selectivity issues, challenging assay designs and incomplete or invalid secondary test cascades. Many of these targets can be modulated by antibodies or other macromolecules. However, this comes at the expense of parenteral application, which is considered less attractive for many therapeutic areas, not to mention the limitation to extracellular targets.

Hence, the future of Medicinal Chemistry will depend on our ability to find lead structures also addressing poorly tractable targets and to optimise them into (oral) drugs with a high chance to demonstrate reimbursable differentiation in clinical studies. The obvious mismatch of increasing risk in the early stage versus excessively high expectations at the end of the R&D process will require adapting the standard throughput models for industrial drug discovery towards longer cycle times and increased resources per project.

In the context of these challenges, even more attention will be attributed to the areas of target identification/validation and to novel, innovative lead finding approaches. Worldwide, several public-private partnerships have been initiated to improve the environment for innovation in these areas. As an example, the European Lead Factory has been recently launched by an international consortium of 30 partners supported by the European Medicines Initiative, the world´s largest public-private partnership in the healthcare sector. The European Lead Factory provides researchers in academia, small businesses, patient organisations and large pharma companies with unprecedented opportunities to jointly discover new drugs through access to a high-quality screening collection of half a million compounds.

The organisers of the RICT meetings have been able to advance the conference in recent years to one of the most attractive annual Medicinal Chemistry events with an excellent diverse mixture of lectures from industry and academia with an appropriate presentation of chemical structures. Target identification/validation and novel lead finding approaches will be central topics at the 49th RICT meeting 2013 in Nice. Hit-to-lead strategies, multidimensional lead optimisation, ADMET and case studies also on less tractable targets such as the sodium-calcium exchanger (NCX) complete the appealing programme.

Prof. Joachim Mittendorf
Bayer HealthCare AG
Germany