PARTNERSHIPS IN DRUG DISCOVERY AND DEVELOPMENT BUILD SUCCESS

A conversation with **CRAIG JOHNSTONE**, Global Head, Integrated Drug Discovery, Evotec

Evotec provides a full range of services to foundations, charities, biotech and pharmaceutical companies, from early drug target identification and validation through hit-finding and molecular optimisation to clinical translation. In August 2017, the company acquired Aptuit, a company with drug discovery, development and manufacturing expertise. Following the acquisition, Evotec launched INDiGO, a system to bring drug candidates from discovery to the point of filing an Investigational New Drug (IND) application.

What are the problems of having separate drug discovery and development processes?
One of the downsides of having discovery do its job and then hand the results 'over the wall' to development is of misaligned scientific and managerial objectives. The timelines of the different functions are quite different: in discovery, cycle times need to be short and agile to create knowledge and learning; in large organisations, development timelines can be long - the entire process can be 12 to 15 years. These differences have an impact on the perceived importance of one month, which can lead to a misalignment of planning and priorities. As a result, the speed with which the valuable asset moves is compromised, and important information is lost in handovers.

How does integrating discovery and development improve the process?
If, during discovery, a researcher is already thinking about the needs of the development phase, they will have heightened awareness and foresight. They can anticipate the risks and build quality into both the molecule and the data package to enrich the probability of success and the speed through clinical development. In contrast, if liabilities appear only after a researcher has handed their molecule "over the wall", it's too late to modify the structure of the candidate.

Discovery is the inventive phase of drug design, when there are many opportunities to change the path forwards. If a researcher knows what the problems are likely to be, they can design them out. This requires thinking about downstream issues such as safety and biomarkers. They should consider the translational-biology plan: what will be measured in the clinic, and how this can be replicated and modelled in the discovery phase. Working in this way builds a more coherent scientific logic earlier on, and anticipates the issues in development. The molecules that the researcher is working on in optimisation can be viewed as prototypes for development — and prototypes can be used to reveal development issues at a much earlier stage, at a point where it's quicker and cheaper to make a change and solve the problem.

How do you insert that development thinking into the discovery phase?
It is important to have many, very experienced drug discovery and drug development people working together. Often the most difficult problems which arises, are not bounded by the classic scientific disciplines such as chemistry or pharmacology. These problems require contributions from across the disciplines to come up with the best integrated solution.

The trick is to acknowledge that drug discovery is a team-based, interdisciplinary activity. Although everyone comes from a particular scientific background and brings discipline expertise, they still need to have a good understanding of the other functions of drug discovery. By working together in this integrated, interdisciplinary way, they will come up with the best solutions to the problems they face. Building that knowledge and experience involves recruitment and then ongoing training and development, but also depends on leadership and expectation setting. At Evotec, we encourage, reward and acknowledge this collaborative and cooperative culture. We are humble to the fact that these are very difficult scientific challenges, and no one person has the answer.

What is INDiGO and how does it fit in with these ideas?
INDiGO is a carefully integrated package that starts near the end of the classic discovery phase and continues to the filing of the IND. It brings together a team of people who are very experienced at taking a drug forward towards clinical development. It covers how the drug is prepared at larger scale, formulated, and taken through regulatory safety testing, ready for human testing. INDiGO also prepares the IND document for electronic submission. By interleaving the manufacture of the drug with an escalating progress through the regulatory safety processes, we have been able to reduce the time that it takes to go from the end of discovery into the development phase. We can take a candidate through to IND in less than 12 months, whereas it could be as much as double that in the past.

Another advantage is that our partners have one point of contact and one set of contractual obligations. We believe that INDiGO not only increases their probability of success, it also makes life much less complicated.

Is this a new way of thinking about drug discovery?
We believe that the drug discovery process is a continuum of solving problems to build quality and success for clinical development. That means smoothly transitioning out of discovery through INDiGO and being ready for the clinic.

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