BIOBUSINESS BRIEFS

DEAL WATCH

Valuation benefits of structure-enabled drug discovery

Valuations of projects in the pharmaceutical industry rely heavily on discounted cash flow methodology, using decision-tree analysis to account for the high attrition rates at each stage of the pipeline — particularly in transitions between clinical trial phases. Increasingly, useful data are becoming available for these attrition rates, which take into account molecule type, originality, therapy area and developer size, and cover Phase I trials through to (and beyond) market approval. However, the discovery and preclinical stages are poorly addressed by current publicly available data.

We wished to investigate whether the availability of protein –ligand structural information for a drug target might have an impact on project valuations, on the basis that such information may enable the generation of preclinical candidates with improved drug-like characteristics and thus a greater chance of success compared with those candidates that are generated for targets that lack such information. We therefore selected 20 targets with active drug discovery programmes: ten diverse enzyme targets for which specific structural information is available and ten G protein-coupled receptor (GPCR) targets for which such information is much more limited (FIG. 1). The Thomson Pharma database was then used to search for both the number and status of all projects addressing each target set by development phase, from discovery through to the launched product.

In total, over 1,000 drug projects were identified: 614 from the structure-enabled enzyme target category and 481 from the GPCR target category. With the aim of removing bias related to characteristics of the targets — other than the availability of structural information — the ten targets within each set were chosen so that the total number of launched drugs against these targets were similar overall: 13 for the structure-enabled group and 14 for the GPCR group.

If the approaches had similar probabilities of success, then we might have expected to see similar attrition rate profiles throughout the pipeline stages, when these were normalized as a percentage of all drugs in the category. However, a striking difference was seen in the total project 'failure' subsets (for example, 'discontinued' or 'suspended' subsets), regardless of development stage; 70% (338) of projects in the GPCR category compared with just 44% (267) of the projects in the structure-enabled target category resided in the failure subsets (FIG. 1). Furthermore, at the time of our analysis (November 2010), the increased proportion of active projects for the structure-enabled targets is most evident at Phase I (FIG. 1), with over three times the relative proportion of projects (9.3% versus 2.9%). It will be interesting to see whether an appreciation of this trend translates into significantly higher valuations for projects on structure-enabled targets that are currently in the discovery and/or preclinical stages, based on a higher probability of these targets reaching Phase I trials.

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M.C. declares competing financial interests: see web version for details.

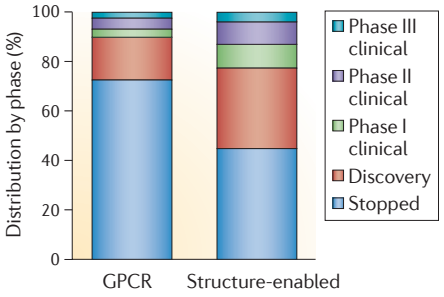

Figure 1 | **Distribution of selected projects by development phase.** The chart shows the greater proportion in active versus stopped projects at different pipeline stages for a group of ten structure-enabled enzyme targets compared with ten G protein-coupled receptor (GPCR) targets (see Supplementary information S1 (box) for target lists). Source: Pharmaventures analysis of the Thomson Pharma database.