

EXTERNALLY SOURCED COMPOUNDS ARE MORE LIKELY TO FAIL

CMR INTERNATIONAL

CMR International, the global leader in pharmaceutical R&D metrics and benchmarking, investigates the productivity crisis facing the pharma industry.

Across the pharmaceutical industry, companies have sought to bolster and strengthen their pipelines by licensing external innovation. Indeed, the increased use of licensing and external sourcing of compounds has become a key strategy for most large pharmaceutical companies, to the extent that a large proportion of their pipelines now originate outside of in-house R&D departments (FIGURE 1).

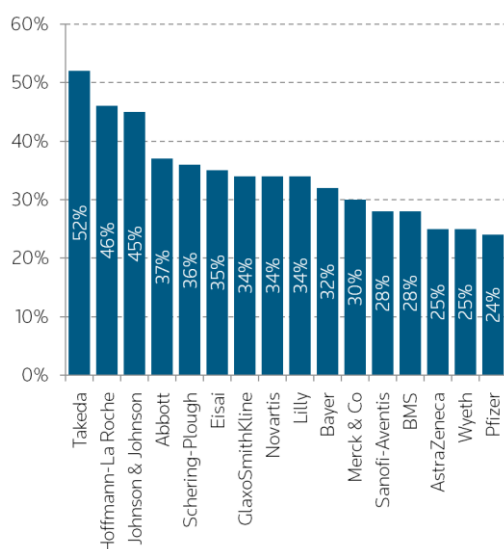
Companies are realising that they are not able to cover all targets and

disease areas internally and so are using partnerships as well as straight acquisitions to gain access to new opportunities. This is also proving to be a fertile area for the development of new business models (for example the Center for External Excellence in Drug Discovery (CEEDD) at GSK) which aim to build mutually beneficial partnerships for early lead development.

This growing dependence on externally sourced innovation is likely to increase as the culture in R&D organisations becomes less internally-focused.



FIGURE 1: PROPORTION OF TOP PHARMA PIPELINES REPRESENTED BY IN-LICENSED PRODUCTS (MAR 2008)



Source: Parexel Biopharmaceutical R&D Statistical Sourcebook 2008/2009

According to Ernst & Young's *Beyond Borders Global Biotechnology Report (2008)*, the potential value of strategic alliances topped \$27bn in 2007 (for biotech-pharma and biotech-biotech alliances). This is an increase over the previous year, which in itself was a record for the industry. All in all, there were eight alliance transactions with potential deal values each in excess of \$1bn, according to the report.

Similarly, many large pharmaceutical companies have acquired entire pipelines as a way of inorganically growing their development portfolios and to access expertise in new science and technology (e.g. NBEs). For example, in 2007, AstraZeneca acquired MedImmune for \$15.6bn, Eisai acquired MGI Pharma for \$3.9bn and Amgen sought to bolster its pipeline

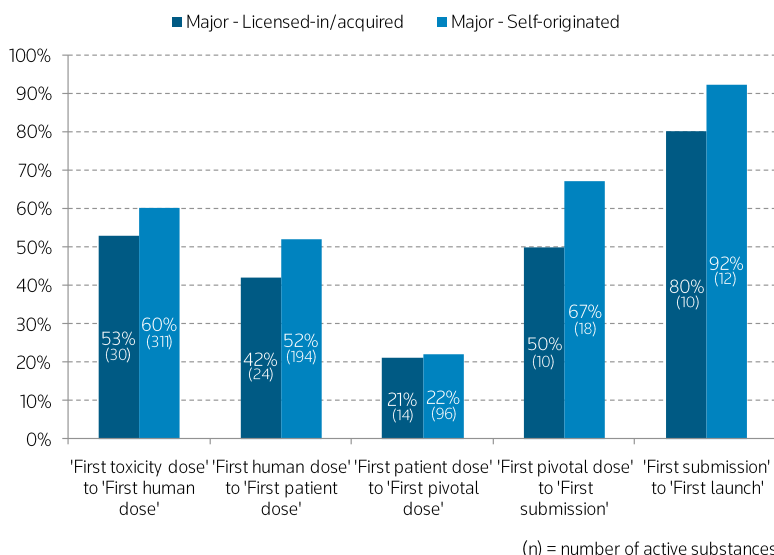
by acquiring Ilypsa for \$420m and Alantos Pharmaceuticals for \$300m.

Externalisation is clearly a commonly adopted strategy in R&D, but is it working? Are in-licensed compounds more or less likely to fail when compared to self-originated drug candidates?

Our analysis of the CMR dataset for 2008 reveals a marked discrepancy between the performance of in-licensed and self originated compounds.

We examined the success rates for the major company cohort (which, within the CMR data set, accounts for the majority of in-licensing volume) and found that in-licensed active substances developed by major companies fail more often than self-originated compounds, in particular at phase III and submission (FIGURE 2).

FIGURE 2: SUCCESS RATES BETWEEN KEY MILESTONES FOR THE MAJOR COMPANY COHORT, BY ORIGIN



We then looked at the trend over time in between-phase success rates for in-licensed compared to self-originated active substances for the major company cohort. Historically, in-licensed compounds enjoyed relatively

higher success rates in early development (FIGURE 3).

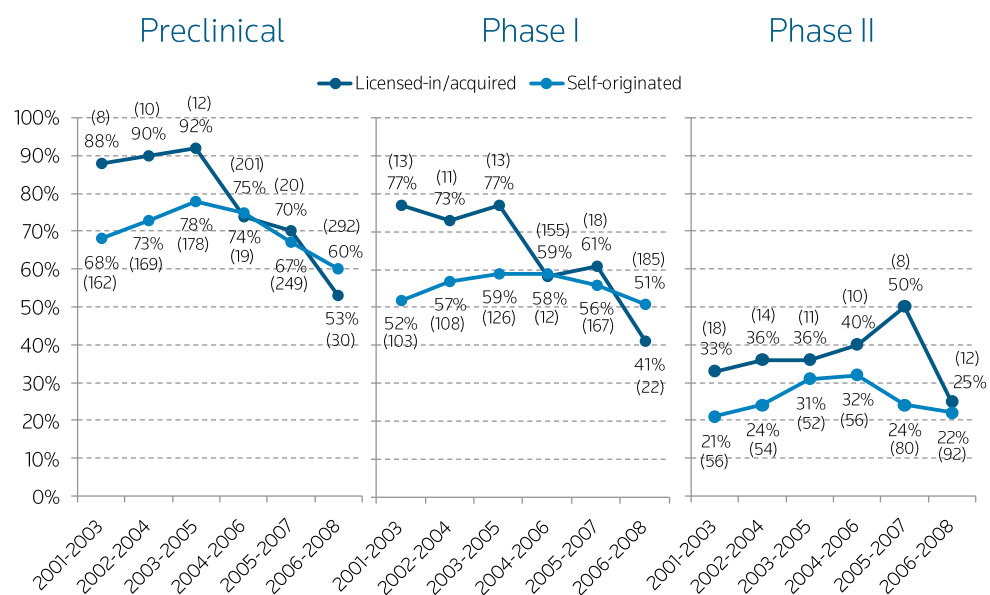
However, this optimistic picture did not translate into higher late development success rates which have consistently been inferior for in-licensed versus self originated compounds (FIGURE 4). In recent years, the gap in early development success rates has narrowed considerably, such that active substance origin now has little influence on this measure.

These trends are suggestive of two potential factors. Large pharmaceutical companies may be becoming more effective in introducing rigor into their scouting and due diligence processes, such that the quality and potential of the in-licensing candidates is improving. Alternatively or additionally, more objective decision making in early development may be ensuring that fewer unsuitable candidates are progressed to phase III.

Whichever of these may be the case, trend analysis of late development success rates for the major cohort indicates that these potential benefits are not yet translating into improved commercialisation. In fact, the probability of successful transition from phase III to submission for in-licensed compounds has trended steadily downwards in recent years and absolute success rates remain notably less than for self-originated candidates (see FIGURE 4).

The industry's desire to look beyond its own laboratories to access innovative science makes sense, but we suggest that the execution of externalisation strategies within development has been and remains sub optimal. Major companies need to be thorough in their due diligence – getting caught up in the race to complete the deal should not stand in the way of a thorough, objective analysis of all aspects of the asset (clinical, commercial, financial, technical, regulatory). Furthermore, they need to apply decision making criteria to in-licensed compounds which are equally

FIGURE 3: EARLY DEVELOPMENT SUCCESS RATE TRENDS FOR SELF-ORIGINATED VS. IN-LICENSED COMPOUNDS FOR THE MAJOR COMPANY COHORT



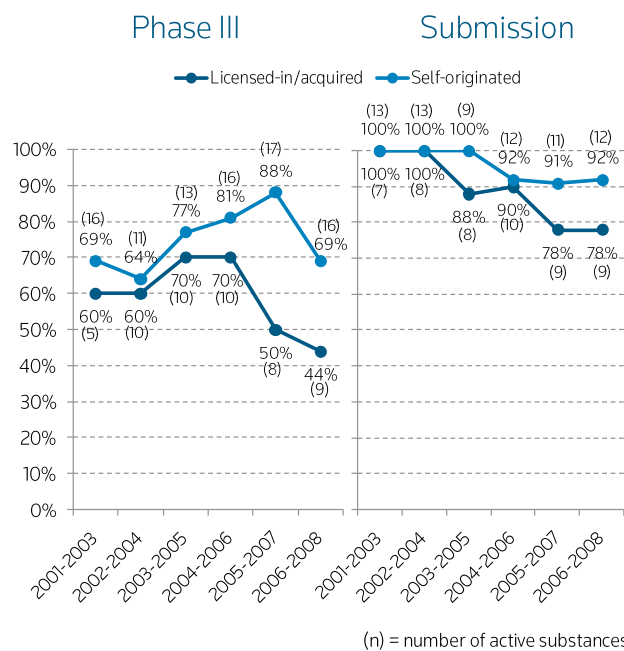
(n) = number of active substances

as rigorous as those for self originated compounds.

The CMR trend data indicates that companies are learning from their experience in early development and are bringing the success rates for in-licensed compounds into line with the attrition rates for self-originated compounds.

However, large companies must continue to focus on improving due diligence and early development decision making if they are to address the continuing gap in phase III success rates and maximize their return on investment from externally sourced innovation.

FIGURE 4: LATE DEVELOPMENT SUCCESS RATE TRENDS FOR SELF-ORIGINATED VS. IN-LICENSED COMPOUNDS FOR THE MAJOR COHORT



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