2013 CMR INTERNATIONAL PHARMACEUTICAL R&D FACTBOOK

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CMR OVERVIEW

CMR International, a Thomson Reuters business, is a world leader in global pharmaceutical research and development (R&D) performance measurements. For over 17 years, CMR International has worked with the leading global pharmaceutical and biotechnology companies to assess R&D productivity and provide insights, which are used to strengthen planning and execution across R&D functions.

We provide our clients with accurate, trustworthy performance metrics and industry benchmarks. Our clients use this information to make critical decisions on how to:

- Stay competitive and compare their overall R&D performance to their peers
- Optimize their R&D portfolio and strategy based on our therapeutic-area specific project durations and success rates information
- Create realistic targets for R&D projects that will motivate and challenge their organization
- Refine clinical trials and patient enrollment strategies based on unique country and site intelligence provided by participants in CMR International's annual programs and focused performance metrics modules

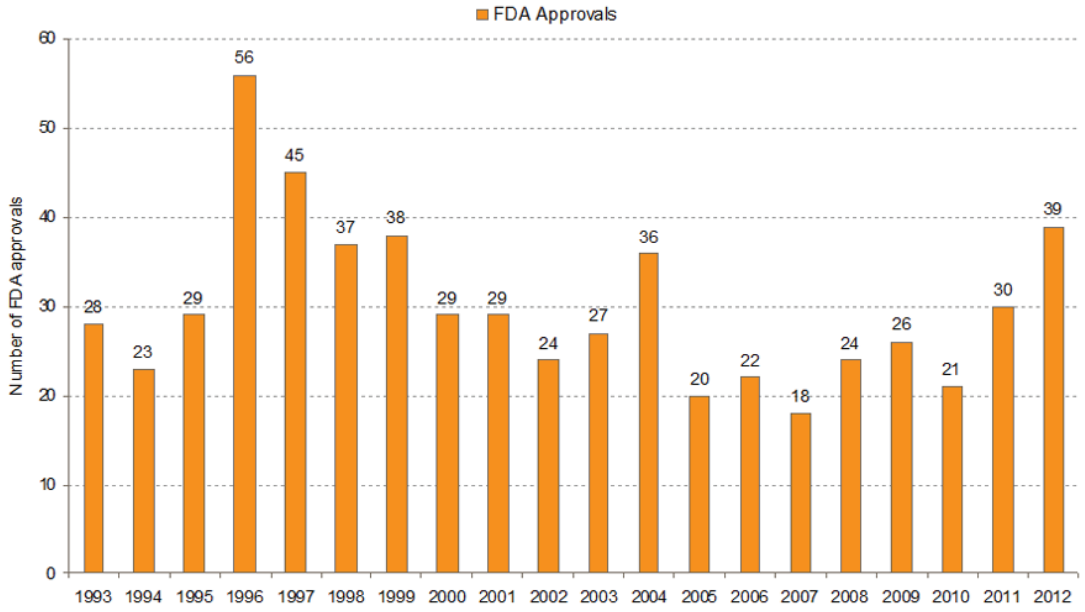
Our experience, independence and integrity—in combination with our dedication to providing the highest quality information, insights and opinions—makes us an essential service for the world's leading pharmaceutical innovators.

EXECUTIVE SUMMARY

Introduction

Despite some rather bleak assessments of global R&D productivity made by commentators across the pharmaceutical and biotechnical industry, the number of FDA approvals hit a 16-year high for a total of 39 NDA and BLA approvals in 2012.

Figure 1. NUMBER OF FDA APPROVALS PER YEAR BETWEEN 1993 AND 2012



Source: fda.gov

Key metrics identified in the 2013 CMR International Factbook indicate a number of encouraging trends across the pharmaceutical industry over the last 10 years including:

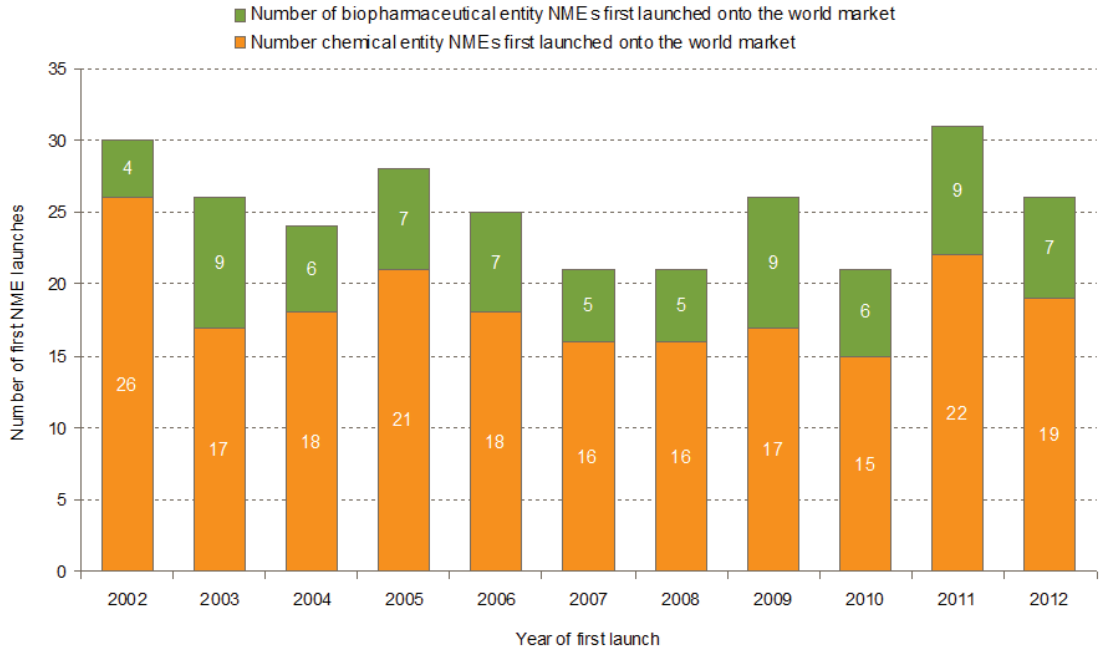
- An above-average number of New Molecular Entity first-world launches in 2012
- A rapid decline in overall development time from 2010 onwards
- Recent growth in the volumes of compounds entering Phase III, coupled with the continuing decline of Phase III terminations
- A 9 percent global ethical biopharmaceutical sales growth rate between 2011 and 2012; a rate which has not been seen since 2008

New Molecular Entities First-World Launches

In 2011, the total number of New Molecular Entities (NME) launched onto the global market reached a 10-year high of 31 NMEs. Although this number dropped to 26 NMEs in 2012, it's still higher than the previous 10-year average (Figure 2). At first glance, the data appears to conflict with the number of 2012 FDA approvals (Figure 1). One reason for the difference is that a subset of FDA approvals may have previously received approval and subsequently launched in other countries. An example of this is Myrbetriq® (mirabegron), which was approved by the FDA in June 2012 but first launched in Japan in September 2011 under the brand name Betanis®[3,4]. This drug appears in the 2011 NME first-world launches list, but is included in the 2012 FDA approvals list. Another difference is derived from a subset of FDA approvals, where the FDA approval is the first globally, but the drug did not launch by the end of that year. An example is Iclusig® (ponatinib), which was approved by the FDA in December 2012, but not launched until January 2013[3, 4]. This drug appeared in the 2012 FDA approvals list, but is included in the 2013 NME first-world launches list. Cases of NMEs launching outside of the USA prior to FDA approval, and FDA approvals not launching in a given year, combine to rationalize the differences displayed in Figures 1 and 2.

The 42 NDA and BLA submissions made to the FDA in 2012, coupled with the FDA approvals that did not launch by the end of 2012, will ensure, both in terms of FDA approvals and NME first-world launches, that 2013 will be another positive year for the biopharmaceutical industry.

Figure 2. NUMBER OF NMES FIRST LAUNCHED ONTO THE WORLD MARKET BY MODALITY BETWEEN 2002 AND 2012



Source: 2013 CMR International Pharmaceutical R&D Factbook

Examining the nature of the 2012 FDA approvals and NME first-world launches provides consistent and encouraging messages. Over half of all approved or launched drugs targeted oncology indications or received orphan drug status in non-oncology indications. A number of personalized medicine approaches are also included in the data in addition to a number of first-in-class drugs. These observations provide evidence for the industry's success in re-focusing R&D portfolios into areas of unmet medical need or for highly differentiated drugs--a strategy which not only provides or extends treatment options for specific patient populations, but also helps the industry manage for increasing regulatory and payer hurdles, thereby driving R&D productivity.

Development Times

Overall development times from discovery to launch in 2012 continued to decline from their 2010 peak of 15 years to approximately 12 years. Examination of the trend in clinical development cycle times from first human dose to first regulatory submission illustrates a decline from a peak of approximately nine years to approximately seven years most recently[5]. To an extent, these declines in cycle time can be rationalized by the observations stated above with respect to the nature of the recent drug approvals and launches. As the number of NMEs targeting rare diseases or with orphan drug status increases, their corresponding development times decrease for two main reasons. First, clinical development cycle time may be reduced as a consequence of the limited or relatively small studies required for submission and approval purposes. For example, the NME Voraxaze® (glucarpidase) was approved by the FDA on the basis of a single study which included only 22 patients[6]. Second, the regulatory review and approval timelines for drugs targeting rare diseases or with orphan drug status is likely to be faster than their non-rare counterparts. In 2012, the FDA noted that first-cycle approval rates hit an all-time high at 80 percent, driven in part by reductions in the number of "me-too" drugs[7]. The FDA also noted that 97 percent of all recent approvals achieved their target approval dates agreed under the Prescription Drug User Fee Act [8].

Decreasing development times are positive news for the biopharmaceutical industry. These reductions, however, are most likely driven by the changes in R&D portfolios rather than any significant improvements to overall development approach.

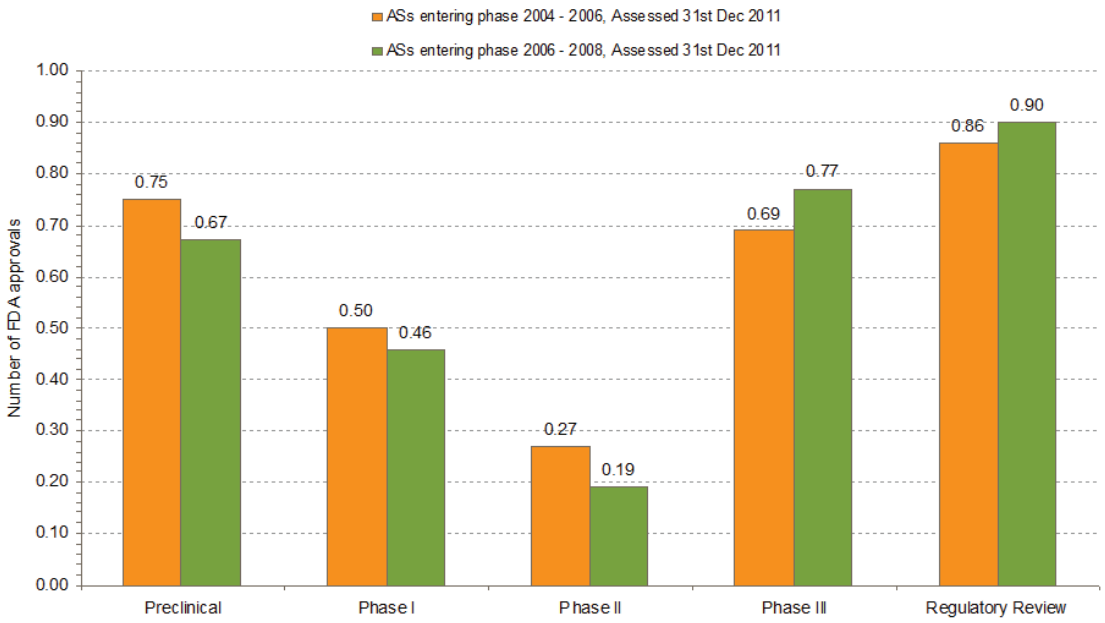
Figure 3. TREND IN DEVELOPMENT CYCLE TIME BETWEEN 2003 AND 2012

Source: 2013 CMR International Pharmaceutical R&D Factbook

Attrition and Success Rate

The number of projects entering Phase III development has increased in recent years and the number of Phase III project terminations has decreased[5]. A comparison of the impact of these two metrics is outlined in Figure 4, clearly illustrating differences in success rates across the two-year ranges and across all phases of development. There is a significant increase in Phase III success that correlates closely to the aforementioned increasing Phase III project volumes and decreasing Phase III terminations. Success rates in Early Development (Preclinical, Phase I and Phase II) have declined during this year range, which at first glance may be seen as a negative message for the industry. Further examination of the reasons for termination across Phase II and Phase III shows increasing proportions of Phase II efficacy failures versus declining proportions of Phase III efficacy failures[9]. Combining termination reasons changes with success rates data does, however, allow for a more positive conclusion. It shows that the industry is designing Phase II programs that are able to support early termination decisions, thereby preventing costly Phase III failures and driving R&D productivity and efficiency.

Figure 4. CHANGES IN SUCCESS RATE BY PHASE



Source: 2013 CMR International Pharmaceutical R&D Factbook

Conclusion

The data presented in this executive summary highlights an industry that demonstrates an ability to respond successfully and improve R&D productivity overall.

The 2013 CMR International Pharmaceutical R&D Factbook contains metrics and analyses on R&D productivity and many other key topics relevant to the biopharmaceutical industry, such as R&D resources and pipelines, patents and generic drugs. For a full list of figures or additional information, please visit our website **cmr.thomsonreuters.com** or contact us using the information below.

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CMR CONTACTS

Phil Miller
Clinical Practice Director
+44 (0) 207 433 4163

Jasmin Mehta
Manager, Insight Solutions
+44 (0) 207 433 4294

The Johnson Building
77 Hatton Garden
London
EC1N 8JS
T +44 (0) 207433 4000
F +44 (0) 207433 4310
info@cmr.thomsonreuters.com

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