



MAKING MARKETS FOR VACCINES

A HISTORIC CALL FOR ACTION

May 7, 2005

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Making Markets for Vaccines – A Historic Call for Action

Across the biopharmaceutical industry as a whole, select companies are pursuing global health research and development but the level of effort is far too limited given the magnitude of need for new and improved drugs, vaccines and diagnostics for neglected diseases. Because of the high market risk, industry and the public capital markets must have meaningful and credible market signals to pursue development of these products, and the financial incentives must be strong enough to compete with other product opportunities. Companies also need to see a clear pathway to get developing world products tested, licensed and distributed to patients who need them. To direct industry's innovations toward the developing world, business opportunities on the scale necessary to attract innovators – particularly the most capable innovators – must be either uncovered or built.

Advance Market Commitments (AMCs), the recent recommendation from the Center for Global Development (CGD), is a significant contribution to the effort to more fully engage the biopharmaceutical industry in solving global health issues. AMCs can increase the value of otherwise insufficient markets, creating incentives for companies to invest their own resources toward products for the developing world. And AMCs can help sponsors leverage their funds by aligning incentives around a neglected disease and encouraging the private sector to compete for the best solution.

BIO Ventures for Global Health (BVGH)* enthusiastically supports the Advance Market Commitment concept. Our aim is to ensure that AMC programs are implemented in a way that is both cost effective for sponsors and attractive to industry's most capable innovators to invest in – and accelerate the development of – innovative products for the developing world. The following comments are informed by extensive conversations with biotechnology executives over the course of the last year and the deep industry experience of our board of directors and business advisors.¹

The Industry Decision-Making Process

Faced with increasing costs and pricing pressures, biopharmaceutical companies are making very difficult choices about which products in their pipeline to pursue with limited resources.² Given the high risk of failure and long development timelines, companies must focus on products that are most likely to generate a high enough return to attract capital. While large pharmaceutical companies tend to pursue development of drugs with market potentials of \$500 million or more

* *BIO Ventures for Global Health (BVGH), a non-profit spinout of the Biotechnology Industry Organization (BIO) with initial funding from the Bill & Melinda Gates Foundation and The Rockefeller Foundation, was formed to break traditional barriers to development, bridging the gap between biotechnology's immense promise and the enormous unmet health needs of the developing world. Our approach is market-based and founded on the belief that economic mechanisms are a critical driver for broad industry involvement in global health product development. Our strength lies in our deep understanding of how industry "works" and our determination to translate that knowledge into solutions that dramatically improve the lives of individuals in the poorest regions of the world. BVGH's aim is to provide equitable solutions to unmet medical needs in the developing world for the benefit of those most in need.*

(and are particularly interested in “blockbuster” drugs with markets exceeding \$1 billion), biotechnology companies are willing to tackle smaller markets, but that market has to be there.³

Companies follow a portfolio approach, measuring and optimizing value and risk for each opportunity across their pipeline. Limited resources (both dollars and staff) force them to make tradeoffs regularly. Companies and investors examine three key risk factors when deciding whether to fund research and development: (1) capital risk (e.g. the cost of product development and manufacturing); (2) market risk (e.g. the size of the market, expected market penetration and competition)⁴; and (3) technical risk (including the likelihood of clinical, regulatory and reimbursement success).⁵

Global health products compete with other projects for funding based on these same factors. Because of the significant perceived risk with developing world products, returns for global health projects must be at least as high as for other investment alternatives.

Barriers to Global Health Product Development

For developing world diseases, lack of credible market opportunities – or information on viable markets – is a significant barrier to entry for biopharmaceutical companies. Biotechnology companies’ reliance on pharmaceutical companies and investors to finance their research and development agenda is critically tied to the convincing demonstration of a potential product’s market viability. In the case of neglected diseases, the limited purchasing power of developing countries and the poor expected return on investment make attracting investment capital or pharmaceutical partners particularly difficult. Many companies operating in this space are able to use publicly-supported grants to initiate an R&D program, but their funding often runs out as products progress through more expensive clinical development.

Further, while direct support (“push funding”) reduces the costs and risks of product development, and has been the driving force behind the increase in new research and development projects, it, alone, will not lead most companies – particularly the more capable innovators – to allocate sufficient resources of their own to fully develop and market these products. It is the underlying market opportunity that ultimately drives decisions. Most companies faced with more profitable alternatives will not pursue developing world projects unless they are seen as significant profit opportunities. If the market is too small, the opportunity cost of allocating resources from the science and management teams is simply too great.⁶

Getting the Market Incentives Right to Attract the More Capable Innovators

Large, diversified pharmaceutical companies have the necessary capabilities to develop and commercialize the bioscience research taking place in public research institutes and biotechnology companies. In fact, most large pharmaceutical companies rely on smaller biotechnology companies to supply a growing proportion of their development pipeline.⁷ Biotechnology companies, on the other hand, range from very small, private companies with few employees to large, public, multi-billion dollar companies such as Chiron and MedImmune. Biotechnology companies, with a few exceptions, are either privately held or have a much lower market capitalization than large pharmaceutical companies and the vast majority are not profitable. For these reasons, the cost of capital for biotechnology companies can be extremely high. Further,

much of the cash for biotechnology companies, especially for more expensive later-stage projects, comes from pharmaceutical companies.

It is both the large pharmaceutical companies and the biotechnology companies with strong management teams, significant cash in the bank or access to capital, with proven product development capabilities that are best equipped to successfully bring new innovations to market. Pull mechanisms such as AMCs can work for early stage projects because large, capable innovators need new products and they will acquire earlier-stage technology to feed their development and manufacturing machine if the market pull is there. Early-stage investors, in turn, invest in companies with products that can be partnered or acquired by large pharmaceutical companies. The value to them comes from proximity to a big market that the company can tackle on its own (which is rare) or from the sale to a larger company because there is a real or, as proposed by CGD and others, an AMC-created, market waiting for the product.

The Creation of New Markets

The creation of new markets will require extensive effort by the global health community, potential sponsors and industry to turn the concept of an Advance Market Commitment into a reality. BVGH has convened meetings and held discussions around global health issues with senior executives from a cross-section of key innovators in the biotechnology and pharmaceutical industry, including those already committed to developing world markets and capable innovators that might be enticed to consider it if the rewards can compete with other opportunities. These discussions and others held with potential sponsors make it clear to BVGH that bringing the parties together around these novel mechanisms will require a sustained activity of education and trust building. Different companies and sponsors will have different key issues. These issues – including those outlined in BVGH’s more extensive discussion document on AMCs – need to be synthesized into solutions that have enough scale on both sides to have a chance of working.

BVGH’s embrace of the Center for Global Development’s report, “Making Markets for Vaccines – Ideas to Action,” recognizes the historic shift in thinking the ideas of the report represent to the global health community. Creating markets for innovative products that address deadly diseases of the developing world is an important step in more fully engaging the biotechnology and pharmaceutical industries in issues of global health. The implementation of these ideas requires continued discussion within the industry if these programs are to succeed in attracting capable innovators and helping sponsors achieve their goals in a cost-efficient and timely manner.

¹ Partial List of Companies Participating in BVGH Meetings and Discussions:

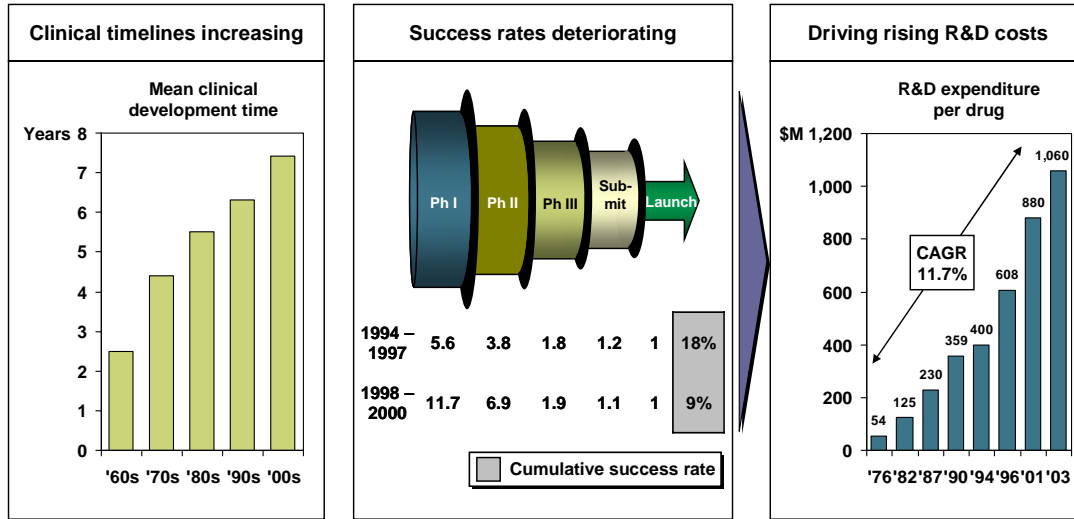
Maxygen
OSI Pharmaceuticals
Chiron
Acambis
Perseus-Soros BioPharmaceutical Fund
AVANT Immunotherapeutics
Hollis-Eden Pharmaceuticals
Gilead Sciences
Genentech
Human Genome Sciences
Burrill & Co.
CV Therapeutics
Genzyme
Targeted Genetics
Vical
AlphaVax
Napo Pharmaceuticals
Baxter Vaccines SBU
GlaxoSmithKline
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Merck
Nabi Biopharmaceuticals
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Leighton Read (General Partner, Alloy Ventures)
Kiran Mazumdar Shaw (Chairperson and Managing Director, BioCon India)

² Drug and vaccine development is extremely expensive and fraught with substantial risks – and both the cost and the risk have been rising steadily over the past three decades. Development of products that make it through to commercialization typically cost between \$100-300 million. However, taking into account failures and the cost of capital, the most recent estimates (2003) put the cost of developing a biopharmaceutical product at upwards of \$1 billion dollars, driven primarily by longer timelines for clinical development and higher attrition rates. At the same time, the market for biopharmaceuticals is exerting much more significant pressure on price.

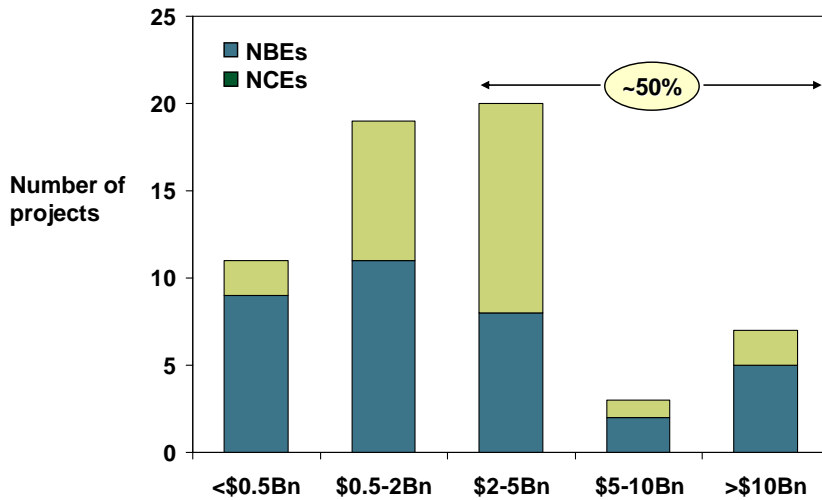
Rapidly Increasing R&D Costs



Source: Boston Consulting Group, Tufts CSDD, Parexel, CMR

³ Analysis of the compounds captured in Pharma Projects Database suggests that more than 80% of the novel compounds currently in phase III clinical development are targeted at markets of more than half a billion dollars.

Target Market Size – Novel Phase III Compounds



Source: Boston Consulting Group, Pharma Projects Database

⁴ For large pharma, expected revenue is \$500 million to \$1 billion per year. For emerging biotechs, the number is still in the several hundred million.

⁵ In the case of AMCs, reimbursement and regulatory risk could include the risk of “changes in the rules”, changes in the “payment situation”, changes in the “success criteria”, and the adjudication process. Payments that are predictable and transparent vastly lower the risk assessment – a critical issue when deciding to start a project.

⁶ Add to this the fact that these diseases are still not well understood, the science is complex, and the prospect of discovering a successful new treatment or vaccine remains risky. For every five product candidates that enter clinical trials, statistically only one will emerge successfully. This combination of high market risk and high technology risk – whether real or perceived – has preempted, indeed prevented, active industry involvement.

Further, sizeable markets alone are not enough. Companies face significant hurdles developing products in uncertain markets where they have limited or no experience. Weak public health infrastructure and distribution systems in these countries make it difficult to test lead drugs and vaccines in clinical trials or get successfully-developed products to those that need them. Navigating multiple regulatory systems to pursue product registration in disease-endemic regions also presents a host of complex challenges. In addition, few adequately understand who the purchasers are and how the procurement process works. To further complicate the picture, the developing world is not a singular concept, so market approaches may vary dramatically by country. Because of all this uncertainty, and the costs involved in developing sufficient expertise to operate in these markets, all but the largest pharmaceutical companies have expressed that developing world markets must be even more compelling than others to lead them to pursue development.

⁷ It has been estimated that as much as 60% of the current pharmaceutical pipeline originated in biotechnology companies.