Arthur D Little

Viewpoint

Funding lower-priority clinical trials

Exploring a new mechanism to fund the timely execution of deprioritized trials

Introduction: Some biopharma companies have built pipelines that offer more development opportunities than their resources allow them to pursue. Promising clinical trials may be moved down the priority list and their execution delayed – resulting in decline of asset value against a fixed patent expiration date. One potential solution is to package complementary trials and bring them into collaboration with the investor, CRO or other organizations and fund the execution of these trials outside the biopharma company. The potential advantages of this approach are four-fold: the trials supporting asset development will be delivered, investors have an opportunity to generate a high return, CROs expand their revenue base and additional patient populations may benefit.

Where are we now, and how did we get here?

A decade ago, as biopharma companies explored strategies to keep growing their product pipelines and businesses, effectively three approaches were identified and adopted:

- Aggressive acquisition (buying pipeline) – e.g., Pfizer (10-year increase in share price – 36 percent)
- Developing new and emerging markets – e.g., GSK (10-year decrease in share price – -24 percent)
- Investing heavily in innovation – e.g., Novartis and Roche (10-year increases in share price – 34 and 25 percent, respectively).

A number of the companies that embarked on the innovation option have been very successful in research and development. These now have to deal with the reality that they do not have the resources to develop each asset in their overflowing pipelines in a timely manner, which leaves lower-priority assets in stasis.

By necessity, biopharma companies allocate their development resources to assets and clinical trials that promise the best return. Building upon common sense and sound business practice, pharmaceutical companies are sophisticated in prioritizing their development dollars. However, the down side of that equation is the opportunity cost of not progressing lower-priority clinical studies.

The value of development assets is based on potential future revenue. The limiting factor to that value is the patent expiration date associated with it. This means any critical path trial that is delayed postpones registration and reduces the value of an asset because the period over which revenue can be earned is shortened.

The impact and scale of this varies from company to company and across therapeutic areas. Companies are employing a variety of strategies and approaches to limit this opportunity cost. Examples of these approaches are trial acceleration (for example, by moving sites or simplifying trial design), limited operationalization and co-development deals with third parties. The last generally takes at least nine months to negotiate, and none of these approaches address the challenge at hand. With more and more focus on the cost of drug development and the price of medicine, this challenge is only growing.

We propose a new way to address this challenge

A partnership model for execution of lower-priority clinical trials would provide a platform to reduce the opportunity costs and lower the threshold for commercial viability. The entity (joint venture, special-purpose entity or otherwise-structured entity) would operationalize and manage the execution of the included trials and require the involvement of multiple parties, notably:

- The biopharma company as owner of the development assets
- One or more CROs for execution of the relevant clinical trials
- Investors: this could be traditional biopharma investors as well as nonprofit organizations with specific objectives in therapeutic areas (such as the Cystic Fibrosis Foundation or Gates Foundation).

It is worth noting that until now we have considered this from the portfolio of one biopharma company. However, it is feasible to structure an entity that brings together complementary clinical trials from more than one sponsor, which would require a few additions to governance but not change the principles that underpin the approach.

The different parties involved and their objectives

The partnership vehicle brings together the biopharma's science and data; the CRO's trial operation capability and capacity; and the investors' funds, along with their knowledge of structuring and exiting these types of transactions. Each party will have its own objectives; the main driver for each of these actors is summarized below:

- Biopharma: Progress a lower-priority segment of the portfolio without increasing demand on development resources
- Investors: Invest funds to generate high returns with a fitting risk profile or otherwise fulfill its mission
- CROs: Increase revenue and client/project portfolio

This particular approach is not suitable for all companies or trials, and requires careful analysis of the portfolio and the assets under consideration, as well as and an understanding of how the clinical trials could be decoupled to enable a valuation of the trial results.

The conditions for this approach to work are: a) the selected clinical trials need to be relevant and complementary; b) there should be sufficient potential value for investors and other participants; and c) there has to be a real transfer of risk from the biopharma to the entity that they do not control.

What do these conditions really mean?

a. Trials need to be relevant and complementary:

- The relevance of a trial is important and reflected in the impact its completion can have on the value of the development asset with which it is associated.
- Trials that are packaged need to be complementary so there is real operational advantage in grouping them and identifying the right CRO to execute them. Complementarity can be in the form of geography, indication, trial duration, patients, etc. – or a combination thereof.

b. There has to be sufficient potential value:

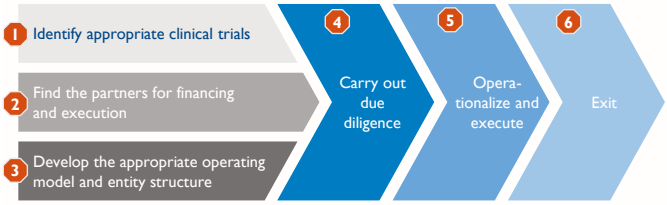
- Upfront work is required in the form of due diligence, financial analysis and identifying the right partners. All parties will be taking a risk, and for that to be worthwhile the combined trials and potential value increase need to be large enough for the various parties to justify the level of upfront work and investment.

c. A real transfer of risk is required:

- One of the reasons this is an attractive model for a biopharma company is that the company gets to develop its assets without adding development costs to the P&L. However, one of the requirements for that to work under financial-reporting standards is that actual risk needs to transfer from the biopharma company to other parties. A clinical trial with a 95 percent probability of success would not satisfy this requirement, as it would just be a financing arrangement camouflaged as an investment.

A six-phase approach from analysis to exit

We have developed a six-phase approach that starts with feasibility and identifying the appropriate trials, and ends with realization of value and exit. The estimated duration of one cycle (an agreed package of trials) is two and a half to three years, though this will likely vary depending on the selection of clinical trials.



Source: Arthur D. Little

1. Identify clinical trials

   a. Develop acceptance criteria

   b. Identify the suitable trials

   c. Analyze relevant trial and asset data, such as probability of success, cost of trial, patent life and commercial profile.

2. Find partners for funding and execution

   a. Identify the appropriate CRO based on required expertise and track record in the specific area

   b. Identify and approach potential investors. These could be VCs specializing in biopharma, non-profit organizations for whose missions these clinical trials have relevance, or other types of investors with interest in the specific area

   c. Consider other potential partners.

3. Develop an operating model and structure

   a. Identify the appropriate legal structure and finance arrangement (which depends on participating companies, countries involved, tax status, etc.)

   b. Develop an appropriate operating model and governance structure

   c. Carry out a full risk assessment

   d. Develop an exit strategy

4. Perform due diligence

   a) Due diligence should be carried out by all involved parties on the relevant aspects of the deal

   b) Due diligence will include:

      I. Technical – does the protocol potentially deliver required data to support an increase in product value?

      II. Commercial – financial components, competitive analysis and market assessment, calculations for valuation

      III. Operational – can we group the trials in question and execute as proposed? Are the proposed trials operationally complementary?

      IV. Cultural – can the partners come together in one vehicle and work well together?

5. Operationalize and execute

   a. Determine location and personnel

   b. Incorporate and activate the entity

   c. Execute a contract with the CRO(s) for clinical-trial operationalization

   d. Implement an operating model and governance structure

   e. Run the operation

6. Exit

   a. In line with the exit strategy determined in phase 3, arrange closing out of the relevant trials, realization of value along contract terms and disposal of assets.

   b. Determine any next steps following out-of-trial results

Case Study

Arthur D. Little developed this model during a project with a major biopharma client. Through portfolio analysis, we identified 33 clinical trials that met the initial criteria for acceptance into this model. The 33 trials represented six different therapeutic areas, and the combined cost of all 33 trials was approximately $480 million.

Therapeutic area	T	II	IIa	IIb	III
Cardio / Metabolic	4	1	2		1
Established Medicines	6	1		1	4
Immunology / Dermatology	7		2	1	4
Neuroscience	6	1	1	1	3
Oncology	3	2		1	
Respiratory	7	3		1	3
Total	**33**	**8**	**5**	**5**	**15**

Source: Arthur D. Little

From this initial list, we selected the respiratory trials (relating to three development compounds and three different indications) and developed a high-level financial model to understand the possible attractiveness of the concept.

The required total investment to run the clinical trials in the new entity was $120M. Based on the underlying asset data we developed a model by building on the current valuation of the asset, as well as the probability of success and impact of the trial (successful or unsuccessful) on the valuation of the asset through adjustment of net present value (NPV).

The outcome of the model was an estimated value increase of $500M over three years on the overall assets. This generates a positive NPV for investors and allows them to double their investment over three years, assuming some of the trials have positive outcomes. This compares very favorably to the return on big biopharma company shares.

Conclusion

The pharmaceutical industry faces many challenges, one of which is an embarrassment of riches in development assets. Some of those assets do not promise the level of returns required by biopharma investors, or would yield levels that are not as high as those of some other assets, resulting in delay of trial execution and erosion of value. Our new, structured approach will enable biopharma companies to continue to develop those assets in an economically attractive way, with benefits for patients, investors, CROs and, of course, the biopharma company.

Contacts

Wilhelm Lerner
Austria
lerner.wilhelm@adlittle.com

Marc Herlant
Belgium
herlant.marc@adlittle.com

Russell Pell
China
pell.russell@adlittle.com

Marcel Hominda
Czech Republic
hominda.marcel@adlittle.com

François Deneux
France
deneux.francois@adlittle.com

Wilhelm Lerner
Germany
lerner.wilhelm@adlittle.com

Vikas Kharbanda
India / Levant Region / Middle East / Singapore
kharbanda.vikas@adlittle.com

Fabrizio Arena
Italy
arena.fabrizio@adlittle.com

Satoshi Ohara
Japan
ohara.satoshi@adlittle.com

Kevin Lee
Korea
lee.kevin@adlittle.com

Guillem Casahuga
Latin America
casahuga.guillem@adlittle.com

Michael Kolk
Netherlands
kolk.michael@adlittle.com

Ulrica Sehlstedt
Nordic
sehlstedt.ulrica@adlittle.com

Wilhelm Lerner
Switzerland
lerner.wilhelm@adlittle.com

David Borras
Spain
borras.david@adlittle.com

Coskun Baban
Turkey
baban.coskun@adlittle.com

Ben Enejo
UK
enejo.ben@adlittle.com

Craig Wylie
USA
wylie.craig@adlittle.com

Authors

Ben van der Schaaf

Special thanks for his contribution Jo Sawyer, Head of External Partnerships, Novartis.

Arthur D. Little

Arthur D. Little has been at the forefront of innovation since 1886. We are an acknowledged thought leader in linking strategy, innovation and transformation in technology-intensive and converging industries. We navigate our clients through changing business ecosystems to uncover new growth opportunities. We enable our clients to build innovation capabilities and transform their organizations.

Our consultants have strong practical industry experience combined with excellent knowledge of key trends and dynamics. Arthur D. Little is present in the most important business centers around the world. We are proud to serve most of the Fortune 1000 companies, in addition to other leading firms and public sector organizations.

For further information, please visit **www.adlittle.com**