The Valuation Of Drug Development Projects—Part 2

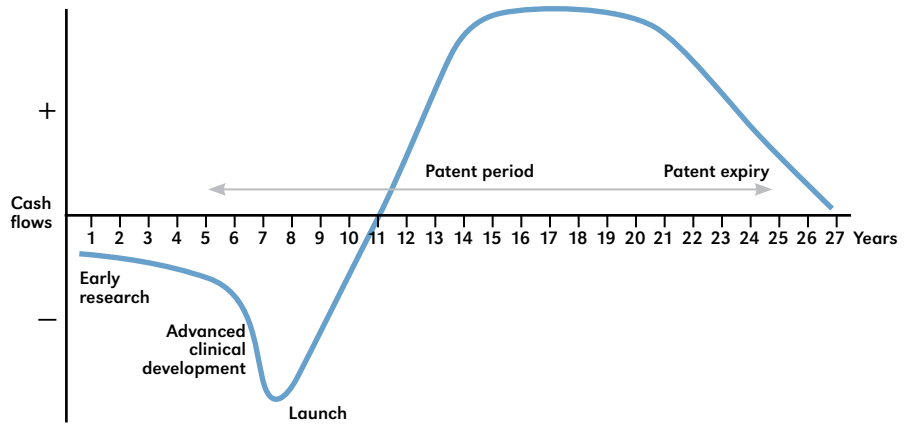
By Sangeeta Puran

Overview

Earlier in March, the author completed a study examining the methods used to value drug development projects. The study was conducted by interviewing individuals over a period of four months[1] in the UK from a representative sample of twelve leading industry participants, including small biotech business development ("biotech"), large pharma and large biotech business development ("pharma"), financial analysts ("analysts") and venture capitalists ("VCs").

The first part of this article[2] provided an introduction to valuation methodologies based on forecasting the cashflows and quantifying the risks associated with drug development and commercialisation. Figure 1 reproduces the previously included example of the typical project lifecycle from a cashflow perspective, starting with early research, followed by clinical development, product launch, market penetration and finally revenue decline after patent expiry.

Figure 1. Example of a Project Lifecycle Curve from a Cash Flow Perspective



We also reported on the methods used by the participants to value drug development projects and considered the VC approach to valuing early stage projects was also explored.

The second part of this article will consider the different biotech and pharma approaches in acquisition, licensing and partnering negotiations. We also consider the valuation approach of analysts setting share prices. Finally, we examine the key challenges in forecasting the revenues, costs and risks associated with a drug development project.

1. Findings On The Biotech And Pharma Approaches In Acquisition, Licensing And Partnering

1.1 Projects On Offer

Participants noted that Phase II and Phase III projects that fit the gaps in pharma portfolios are becoming increasingly rare:

"In the overall deal environment, it is still a tough market for good assets, and Phase III assets that could be launched in a year and fit our profile are not easy to find." (pharma)

Some participants predicted a continuing shift towards early stage deals:

"Note that the number of Phase II deals are going down, with pharma looking at much earlier stage projects." (biotech)

Participants see pharma as increasingly open to considering drug candidates with smaller markets if the end product can be marketed within its sales force machinery:

"Market share is the thing to get right … The key issue from the pharma perspective is: can it get leverage from its existing sales force to the market under discussion? Pharma has the benefit of huge sales force machinery and is always looking to give this machinery more to sell. It also means that pharma may be open to looking at products with a smaller market share." (VC)

Buyers are also considered to be applying more

1. September 2008 to January 2009.

2. The first part appeared in the previous issue of *Les Nouvelles.*

specific requirements to what a product profile needs to look like in order to succeed:

"It is important to consider the product profile—what profile must be achieved to be worth taking to market. Many projects will be terminated." (VC)

"When pharma is looking at things top down within the organisation, standard attrition rates would be used across all therapeutic areas. However, when looking from the bottom up, we are starting to build in very specific attrition rates for that specific drug, i.e. product-related attrition rates. These would take into account whether the drug would be best in class, or first in class, whether there were any toxicology problems etc. These rates would be very different in oncology and infection." (pharma)

1.2 Outright Acquisition

Some participants referred to outright acquisitions of biotech companies becoming more popular than complex licensing and partnering deals. Others commented that the current value for biotech companies running out of funds and with low prospects of independent fund-raising lies in being acquired.

One participant referred to a trend of partnering and licensing negotiations being run in parallel with, or as a prelude to, acquisition negotiations:

"The real game is going on with private companies where no one is actually intending to license because the licensing of lead products will be negative to a future purchaser. So they use auctions on lead products. They use this to push up-front payments and then they will often say 'you are better off buying the company'." (biotech)

"There used to be lots of milestones and royalties. Increasingly small companies are saying 'give us the cash now and you can have the whole thing'." (biotech)

"Licensing is only interesting to VCs if they are in for the long haul and the company has a platform technology or multiple products." (VC)

1.3 Other Arrangements

Pharma participants described receiving renewed requests for loans from cash-strapped biotech partners referring to the possibility of pharma directly re-financing key biotech partners in financial difficulties:

"We have had recent requests from biotechs for loans—acting as their bank. This may be substituted for an equity stake. I think we will see loans and equity stakes again." (pharma)

Participants considered the current market circumstances to have revived interest in the acquisition of minority equity stakes in biotech and pharma partnering arrangements:

"Minority equity stakes are increasing but in the current market there is the insolvency risk and more concern in the financial stability of the biotech partner." (VC)

Views expressed outside of this study also point to greater interest on other deal structures, including recent attention on the acquisition of options to acquire drug development assets (instead of the outright acquisition of the assets). The option deal structure, whilst considered disadvantageous from the biotech perspective, is reported as being considered by rights owners unable to otherwise access necessary funding.

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1.4 Sources Of Value Discrepancy

Participants also provided examples of the sources of value discrepancies between rights owners and buyers in price negotiations.

- Differences of opinion with respect to risk, time frame, future investment, etc.

The guess-work and subjective assumptions involved in predicting key inputs provide an obvious source for value discrepancies. Most participants agreed that discussions over assumptions and forecasts have the potential to continue indefinitely.

- Differences of opinion with respect to the stage of development

Pharma participants reported encountering overestimations of the true stage of development, meaning that a buyer would have to re-do development work, which in turn leads to a delay in development and complicates analysis of competition at launch:

"A biotech will tell you they are risk-taking and can quickly develop the products. When you get to the biotech's Phase III product, you discover you have to re-do the work and this is where due diligence is important in determining development overestimation and value." (pharma)

"Biotech companies have the attitude that they knew they were going to have to partner so that they would do the least to cause harm to their products and get them through to Phase II, when they would have a value. In contrast, we would have done trials across a range of things. The biotech's whole driver would be keeping the product clean –'innocent until

proven guilty'- whereas ours was quite the opposite i.e. 'guilty until proved innocent'." (pharma)

Other participants thought that development overestimation should be less of an issue in the view of regulators (including the U.S. Food and Drug Administration) providing greater guidance throughout all phases of clinical development.

- Different strategic considerations and negotiating power

The theoretical value derived from applying quantitative valuation models, when considered in isolation, assumes that the drug candidate/project has an intrinsic value. The participant responses indicate that, while one may argue over the assumptions and forecasts underlying the inputs of a quantitative model, the price of a drug development project ultimately depends on overriding qualitative factors and subjective criteria specific to the biotech rights owner and the pharma acquirer/partner:

"The official version is the perception of risk and need for future investment. The unofficial version is how desperate they are for the deal, and how much they can do over the other side." (biotech)

"There is a difference of opinion with regard to the risk, time frame, likelihood of dilution moving forward. The overriding point is who wants/needs it more?" (analyst)

The strategic factors and synergies that the particular acquirer or partner may wish to exploit in connection with a drug development project are critical to what the project will be worth to the pharma acquirer or partner:

"Valuing a partly developed project should be for a reason. If it is to sell the programme to a partner, it can only be a starting point. Purchasers will pay what they need to strategically (which is not the same as NPV)." (VC)

"Negotiating power is all-important when a small company is being bought. This usually boils down to financing risk—will the company shortly run out of money and what are the prospects for further independent fund-raising? The other party would not be targeting if the fit was not appropriate." (corporate finance)

Cash flows, together with the prospect of independent fund-raisings, were identified as factors determining what the project will be worth to a biotech rights owner:-

"Biotech is less interested in NPV and more interested in upfronts and cash flow." (pharma)

"A biotech is concerned with its cash flows and getting to the next point. In comparison, pharma approaches valuation by reference to the big pipeline world …" (pharma)

One biotech participant was keen to highlight that cash flows will be less relevant to a cash-rich rights owner:

"If a biotech has loads of cash then it may be less interested in upfronts. The pharma view stems from being margin conscious and not cash conscious. So you have this bizarre thing of sales-based milestone. Sales-based milestones do not affect the margin of the product. Also, the headline value of the deal can be increased by using sales-based milestones. Also from the perspective of a biotech, if you are in survival mode, then the NPV in 15 years is irrelevant." (biotech)

1.5 Project Value Splits

Participants were asked to comment on the typical value split between rights owners and buyers. A limited number of participants acknowledged typical NPV splits:

"In the early stages, the typical split is 80/20 in favour of the licensee. If the product is in Phase III, the licensor will be looking for around 60-70 percent of the NPV." (pharma)

"In relation to value split note the following: 90/10 (licensee : licensor) split for early stage; 75/25 (licensee : licensor) for Phase II; above Phase II, 50:50 (depending on who takes on the development costs)." (biotech)

However, most participants were reluctant to acknowledge any typical split, preferring to treat each deal on a case-by-case basis:

"There is no definitive answer on this as it depends on the stage of the project, the size of the upfront payment (if any), who pays future development costs and whether the licensor retains exclusive marketing rights for any territories. It also depends on whether it is a competitive bidding process (which is ideal). The likely best outcome for a licensor with a product at pre-registration will be a 25 percent royalty on sales with some sort of upfront calculated as a percentage of estimated peak sales." (corporate finance)

"I am not sure there is a 'typical' split. If you want to take a broad brush approach to it this would probably be different depending on drug/device stage of development, etc." (analyst)

"Each deal is an individual discussion." (VC)

The participant responses also identified factors that influence the allocation of value as between

rights owner and buyers.

- Innovation:

"The innovation step is critical so, even if you have not spent money on development, if you have created a huge market value potential, then there will be a royalty greater than 20 percent." (pharma)

- Risk assumed by a party:

"Risk is key…if the mechanism is known, if the product is in lead, if it is close to market, you pay more." (pharma)

"If the product is early stage, the licensor would expect a much bigger split because they are taking the risk. At the late stage, they would generally use 50/50 as a starting point. These percentages are not definitive." (pharma)

"For a brand new product and an immature market, more risky." (pharma)

- Extent to which downstream costs and responsibilities are shared:

"Milestone payments are calculated by reference to how much you pay for development. If the payee contributes more, then the milestone payments get bigger." (consultant)

"The ability to fund late-stage clinical trials always limits cost sharing for a smaller company, thus balancing the NPV equation. The rest is basic economics on opportunity cost (upfront payments) and the risk of cash flows not arising or being delayed (given an uncertain regulatory environment)." (corporate finance)

"Biotechs pretty much always ask for co-promotion which would help their valuation." (pharma)

- Whether the rights owner is seeking to retain any rights or has already out-licensed any rights (e.g. exclusive marketing rights for any major market) is clearly key. One of the participants referred to the acquisition of ImClone by Eli Lilly in 2008, where much attention focused on the fact that ImClone had already granted to BMS the rights to ImClone's blockbuster cancer drug, Erbitux.
- Where the payment structure comprises relatively larger upfront payments and smaller late-stage payments, the buyer clearly assumes more risk. Consequently, the buyer will typically require a larger percentage of the project value. The participant responses offered explanations on why this was generally advantageous from the rights owner's perspective:

"From the perspective of the licensor, it wants everything now because it wants the cash flow." (consultant)

"Cash today is almost always preferable for a small company even if it reduces the overall retained proportion of the NPV." (analyst)

"For a small drug discovery company, it is all about how soon can you get hold of cash that is not committed to something else (i.e. Glaxo paying you £1 million to hire £1 million worth of biologists to work on a project is not helpful. Them paying £2 million to hire £1 million worth of biologists gives you £1 million spare)." (biotech)

"Hedged—very sure of the value in the product and close to launching." (analyst)

Notwithstanding, the obvious advantages for a rights owner of a frontloaded payment structure, participant responses also highlighted the downsides of such a payment structure that a rights owner needs to consider, including:

- Reduced share of the total deal value:

"The obvious downside for the buyer and upside for the seller of upfronts is that the cash is handed over whether the project is a success or not. The upfront will be much smaller than the total deal value if the payment is deferred." (biotech)

"An early stage licensing deal will only attract low to mid single digits. Phase IIa complete may get high single digits. Phase IIb complete may get low to mid teens. A high upfront payment (getting rarer) will always reduce the royalty rate." (corporate finance)

"If the licensor is seeing it as a financing option to develop a subsequent pipeline, a high upfront payment will be sought, to the detriment of the royalty. If the licensor is well funded, they are more likely to retain a higher royalty rate." (corporate finance)

- Even if a buyer agrees to a frontloaded payment structure, buyers are currently less willing to agree to high upfront payments:

"Licensees appear to be less willing to agree high upfront payments." (corporate finance)

- High early milestone payments may skew a buyer's decision against the continuation of a drug development project. This is relevant to scenarios where the payments to be made to the rights owner are contingent on the buyer progressing development and meeting future milestones:

"One must look at the economics. Often, negotiating parties ignore that people have to make decisions. For instance, if you have a small company with a programme in early stage development and

it is negotiating with a large moderately capitalised company (not as big as a pharma company) and the research is in one of those areas where you have got good Phase II data to date, the small company knows that the R&D will work and will commonly negotiate on the basis that, when it gets through, they will get a really big milestone payment. This position could skew a decision against your product. Therefore, you must put yourself in the shoes of the other side and consider what the decision process will be. The product may be returned and therefore you have to also consider the value if the product/ project is returned." (biotech)

- Competition amongst bidders:

"The licensor share is driven by competition. We would of course not offer more unless we had to, e.g. if we were at risk of losing the deal. We would tend to work up the initial valuation in 'exquisite detail' then go in with a bid, and competition would change everything. It is a question of 'how hungry are you?' Passion takes over from common sense. For example, where there is an important strategic gap in the portfolio, the price would go up—but one would not start from that position." (pharma)

"Competition is a key driver. A high upfront payment is more likely if a bidder perceives it must pay this to secure the licence." (analyst)

Notably, a biotech participant pointed out that the deal structure is also relevant when evaluating value allocation between the parties:

"From the perspective of biotechs, in the case of auctions you tend to get the position flipped with pharma saying 'your product has huge sales potential' but when you look at the deal structure this is not the case. So, for example, if you take a $2 billion product and pharma says 'we will give you huge sales milestones ($500 million etc)' but at the same time pharma is not agreeing to pay high royalty rates in the early stages of sales (for example, if you get a low royalty rate up to $200 million) this indicates that pharma does not think that the data or the product is as good." (biotech)

2. Findings On The Analyst Approach

Financial analysts apply valuation tools as part of setting share prices. The analyst participants confirmed that they are mainly interested in late stage projects with many analysts placing no value on pre-clinical projects, and some taking a more extreme approach:

"We give anything prior to Phase II a value of zero." (analyst)

The analyst approach was explained as stemming from the high risk associated with early stage projects. Once interest in a project is registered, the analyst will focus on when the drug candidate will be launched and when relevant sales will peak.

According to a biotech participant, this approach ignores that the present value for biotech companies currently lies in being acquired. If an early stage project is of interest to an acquirer, then the acquirer will place a positive value on the project, whereas the analyst approach may assign no value to it at all:

"What they should do is to actually give anything beyond Phase II a value of zero. The analyst view is based on the business model of licensing being the main route of commercialisation. Note that the number of Phase II deals is going down, with pharma looking at much earlier stage projects.

The present value for a biotech lies in being acquired and not in doing licensing deals. Therefore, the value to an acquirer is completely different.

For example, consider the scenario where you have a company with the following products: Phase II diabetes product; Phase I cancer product; Preclinical platform for other metabolic disorders; and Pre-clinical platform for inflammation product.

The analyst will ignore the pre-clinical platforms. The analyst will do an NPV on the products. The analyst will do a licensing deal on NPV and add these all up with the cash that the company has and give you the value of the company.

If the company is bought by a company that is looking to get into metabolic disorders then the Phase II deal for diabetes (which analyst has given most of the value) is irrelevant. The acquirer will place a positive value on the metabolic pre-clinical platform and possibly put a negative value on the cancer product.

Analysts really get it wrong and the one thing they get paid to do, they don't do, that is, look at what are the chances of the product succeeding?" (biotech)

3. Forecasting Challenges

Participants were asked to comment on the key challenges in forecasting the future revenues, costs and risk associated with a drug development project. They were generally comfortable with their ability to estimate the costs of drug development. In comparison, significant uncertainties existed around projecting revenue and risk parameters. The emphasis on revenue potential and risk is consistent with NPV modelling showing the highest sensitivity to changes in these parameters.

3.1 Inputs For Projecting Revenue

The key difficulties relating to revenue forecasting stem from the inability of participants to predict the shifts in, or to control, the factors determining a new product's ability to penetrate a market:

"Sales inputs … pose uncertainty. The greater the uncertainty, the earlier stage of development a candidate is in. For instance, in one project, the therapy area we looked at changed drastically over the space of one and a half years when the drug candidate moved from Phase II to Phase III trials. As a result of changes in treatment paradigms used by doctors (e.g. what drug is used in first line, second line treatment), this directly impacted potential sales for the development candidate." (pharma consultant)

"We feel most comfortable in regards to the things we can control (such as our own expenditure and development) rather than market share and competition (things which we cannot control). Sales forecast is the factor which has the biggest impact, yet over which we know the least, so it is this aspect about which we struggle the most—it is a bit of a 'shot in the dark'." (pharma)

"The reimbursement and pricing landscape are shifting and the value proposition may look attractive now, but turn out to be quite different. You look at the competitor landscape, how appealing it is to end users, the payer's price benchmark, and markets becoming subject to generics/forced reference pricing when one product goes generic." (pricing consultant)

In particular, many participants emphasised struggling with assessing competition:

"You can give best estimates of value given the current understanding of the market and anticipated product competitive profile … but educated guesswork cannot take account of unknown development projects." (corporate finance)

"There are real difficulties in primary care, and competition is difficult to predict … There is a fundamental difference between being first to market and second to market." (pharma)

"Competitive profiling at the time of launch is difficult to predict accurately as it will depend on data from pivotal trials. Should generic competition be a critical issue at the time of launch, the product will require a significant advantage to secure a price premium." (corporate finance)

Despite being perceived by the other groups as possessing informational advantages, pharma participants indicated that they too struggle with predicting parameters underlying revenue and risk:

"For the initial valuation, we will put in standard values to see if it is even worth going so far as to investigate whether there is a business case. Then we will work up a very specific sales forecast (taking into account the competition, the patent situation, etc, although we've never got it right yet. All one can ever do is a 'best guess' and this is where the most heated discussions are, although it is rather a waste of time because no one knows the answer. There are conversations with people saying 'how do you know we're going to sell this?' Everything else can be much more precise." (pharma)

3.2 Determining Risk Parameters

The key difficulty in determining appropriate risk parameters stems from an inability to derive project specific rates:

"The probability of success is very difficult to estimate." (biotech)

"The most difficult input metric to measure is the probability of success, as this often depends on the label sought." (consultant)

"The greatest challenge is with respect to forecasting risk. Halving risk assumptions can effectively double value." (consultant)

Participants tended to rely on industry averages, whilst acknowledging the limitations of using them:

"NPVs are based on standard probability rates and these are industry-based rates which are totally unrealistic. For instance, once one gets to Phase II, some industry rates will say that there is a 30 percent risk … If you take, for instance a cancer product which has a high market value, and a product aimed at a better understood disease with a lower market value, consider which one will actually make money." (biotech)

"The DiMasi data for probabilities of success and timing is getting a bit old but is still industry standard." (corporate finance)

In relation to discount rates, there was a difference in opinion on whether discount rates should be changed in line with changes in interest rates. One participant highlighted the misuse of discount rates:

"Discount rates are not used properly. For instance, discount rates do not necessarily change with changes in interest rates." (biotech)

Another participant defended not changing discount rates on the basis that discount rates are an estimate over the long term life of a drug development project.

The need to consider market risk was also raised:

"Once launched … the product itself can lend itself to differing take-up. Therefore, for example, a biologic which can be controversial may have a slower take-up. Equally, a company that makes the medical device to deliver a drug has other inputs which can provide additional subtleties to the valuation." (analyst)

3.3 Forecasting Costs

The findings confirm pharma's information advantages when it comes to forecasting late stage development and marketing costs. The historical division of responsibilities between biotech and pharma has the latter assuming responsibility for downstream development and commercialisation activities. Whilst pharma understand clinical investment, a pharma participant commented on how it is becoming more difficult to predict what is going to be required of a drug candidate for regulatory approval:

"Clinical investments are well developed in big pharma but regulatory is difficult to predict." (pharma)

The non-pharma participants mainly relied on industry standards and conventional assumptions whilst acknowledging their limitations:

"Costs/timings in clinical trials in highly competitive areas will be difficult to predict as competition for recruitment to trials becomes an issue." (analyst)

The less detailed approach by biotech investors to assessing downstream costs was also explained by the biotech business model:

"The business model is someone buying a biotech company and you are not interested in late stage data. Pharma do not like the way biotech do that." (biotech)

3.4 Forecast Period

Participants saw the key challenge in connection with forecasting the development timetable. Any delays in development have significant implications for the all important competitive positioning:

"Development time is critical. If you lose time, then there is a knock-back effect on competition position and development costs. At one stage the development time was said to be twelve years … now said to be nine years." (pharma)

"It is a given in the industry that everything is going to change and so one usually starts with a joint development plan (either drawn up by us alone if we were going to control it, or jointly between the parties). Within that, there would be a joint committee or our own portfolio review allowing things to shift off the initial plan. I doubt that we (or any other pharma company) have ever done a project to time and as originally specified. If things were to go badly, or warning bells were being sounded (e.g. the product was no longer going to be first in class or best in class), then we would have the right to opt out/to stop." (pharma)

3.5 Pharmaceuticals Versus Biopharmaceuticals Versus Medical Devices

The participant responses also identified differences between pharmaceuticals, biopharmaceuticals and medical devices, with most responses focusing mainly on differences relating to risk:

"Biologics have a different profile, slightly better than NCEs at the early stage but worse at the later stage." (pharma)

"Biologics have lower risk but development takes longer (risk is lower because these are naturally occurring substances and so they already work in some capacity)." (consultant)

"Risk with medical devices is easier to predict as it is often a technical challenge rather than a clinical challenge." (corporate finance)

"A company that makes the medical device to deliver a drug has other inputs which can provide additional subtleties to the valuation. The risk percentages used tend to be different. It is far easier to see a medical device to market than a blue sky drug, therefore your risk adjusted would differ." (analyst)

In respect of the widely acknowledged lower risk profile of medical device development, one participant warned against assessing these lower risks in isolation in circumstances where the development of the device (and its value proposition) is tied to drug development:

"Where the company had been manufacturing drug delivery devices, it was absolutely essential that the device time scale was not the weakest link in getting the product to market. Everyone expected that one could time the delivery of the device to the day because it was manufacturing—although in reality it is tied to the drug." (pharma)

Differences relating to other NPV parameters include:

- Regulatory, costs and timing:

"Compared to NCEs, biologics and medical devices are likely to be different at the level of regulatory, product development costs and timing." (consultant)

"There are differences between (i) medical devices and (ii) biologics and NCEs. The time lines are much shorter for medical devices. In the case of the diagnostic tools, products could be ready within

five years." (consultant)

"It is more difficult to estimate the cost of goods with biologics unless the scaleup pathway is very clear." (corporate finance)

- Sales:

"Once launched … the product itself can lend itself to differing take up. Therefore, for example, a biologic which can be controversial may have a slower take up." (analyst)

End Note

The theoretical value derived from valuation methods, when considered in isolation, assumes that a drug development project has an intrinsic value. Yet, most participants explained deal values simply on the basis of who wants/needs the asset more. Consequently, the key sources of value discrepancy continue to depend ultimately on qualitative factors and the subjective criteria specific to the rights owner and the buyer, and the negotiating power of the parties.

Cash flows, together with prospects of independent fund-raising, are factors relevant to determining what the project will be worth to a cash-strapped biotech rights owner. For a pharma buyer, key factors include strategic factors (e.g. whether the project fills an important strategic gap in the buyer's product portfolio) and the synergies that a buyer can exploit (e.g. whether the buyer can leverage its existing sales force to market the new product).

Therefore, it is important to identify the subjective criteria and qualitative factors relevant to the other side and to address these issues early by having in place strategies and practices that best emphasise relevant criteria and factors.

Finally, competition amongst the bidders is a key driver of deal value and value splits. The pharma participants acknowledged that, whilst they will work on their initial valuation and bid in detail, competition will change everything.

As to the current function of quantitative valuation, the application of valuation tools remains as an important tool by which to gather insights into as many possible sources of value and uncertainty, requiring participants to remain proficient in their approach to valuation. An understanding and appropriate quantification of as many possible sources of value and uncertainty remains important to decreasing the risk of underselling or overvaluing drug development projects. ■