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A report from The Economist Intelligence Unit



The changing biopharma risk equation

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Preface

As pharma companies expand, they are looking more and more to biologics for their next potential blockbusters. However, this class of product—ranging from well-established large-molecule drugs to truly novel therapies—poses major challenges because of their scientific complexity and sophisticated development requirements. Furthermore, expanding the drug pipeline isn't the only growth strategy most companies are pursuing: They are also planning to expand geographically and expect to face various risks doing so, including unfamiliar regulatory environments, shifts in pricing and customers' ability to pay.

All this means that risk management is rising in pharma executives' agendas. To manage risks, companies are developing strategies that involve both building internal capabilities and reliance on external expertise.

This paper, which incorporates the results of a survey of 254 pharmaceutical executives from around the world and a range of interviews with industry experts, explores in detail global pharmaceutical companies' growth strategies and their plans for managing the associated risks.



About this report

The changing biopharma risk equation is an Economist Intelligence Unit (EIU) report sponsored by MilliporeSigma. It draws on a multinational survey conducted in March 2016 of 254 pharmaceutical executives. The respondents represent a range of companies that are currently involved in or planning to engage in biopharmaceutical development.

Half the survey respondents are C-level or equivalent executives; the remainder hold senior vice-president, vice-president or director positions. Of the sample, 30% are North American, 30% are from across Europe, 30% are from the Asia-Pacific region, with the remaining 10% from the rest of the world. Executives at companies of all sizes responded, with 50% coming from companies with global revenues of US\$500m or less, 37% from organisations with \$500m to \$5bn in annual revenues and 13% whose annual global revenues exceed \$5bn.

The report includes insights from a range of pharmaceutical development experts. The EIU would like to thank the following interviewees for their input:

- Steve Bates, chief executive, BioIndustry Association (UK)
- Andrew Baum, managing director of equity research, Citi
- Ralph Marcello, principal, Deloitte Consulting's life sciences consulting practice
- Tom Ransohoff, vice-president and principal consultant, BioProcess Technology Consultants

The findings and views in this report do not necessarily represent the views of the sponsor. The report was written by Sarah Murray and edited by Rebecca Lipman.



Executive summary

Pharmaceutical companies are in an expansive mode. With rapid advances being made in the development of new therapies, including stem-cell derived therapies and gene therapies, and a growing cohort of potential customers in the burgeoning middle classes of emerging markets, expansion into both new product categories and geographic regions is a priority for most companies.

"In many ways, the industry has never had it so good," says Andrew Baum, managing director of equity research at Citi. "It's got great science, helpful regulators and a growing elderly patient population." Steve Bates, chief executive of the UK's BiIndustry Association (BIA) agrees. "People think there's lots of exciting science that can be translated into new products and services."

The survey found that companies are pursuing different classes of new biopharmaceuticals (also known as biologics) as part of their expansion. These drugs fall into two distinct categories. First, large-molecule biologics, such as monoclonal antibodies used to treat chronic diseases including, diabetes, cancers, and rheumatoid arthritis. Although these complex therapies have been in use for more than 30 years and are already well-established, the category continues to experience significant growth based on scientific and technical innovation. Second, novel therapies that are truly cutting edge, such as gene and cell therapies. Therapies in this category are still largely in experimental phases and not readily available to the market. However, expectations of widespread adoption are at the core of many visions of personalised medicine.

In terms of geographic expansion, companies report that they are typically following a two-pronged approach, with a relatively even mix of expecting to grow market share in other countries and expecting to increase production and development capacity there. This is typical for the industry, according to Mr Baum. "If you're a multinational, geographic expansion goes with products in your portfolio—the two are rarely decoupled," he says.

Companies indicate that they plan to add production and development capacity in all global regions over the next five years. The survey also showed strong anticipation for entering Asian markets in the same time period, particularly in Indonesia, South Korea and Taiwan.

Although the mood of the industry is expansive, such advances bring with them a range of familiar and new risks—and companies are aware of a range of challenges ahead. In the survey, the top risks to growth strategy include regulatory uncertainty and lack of investment

funding for growth plans, closely followed by other familiar concerns: willingness and ability to pay for drugs, patent expiration and the emergence of drug categories not within companies' pipelines. The majority of respondents also expect risks associated with new drugs to increase somewhat or significantly.

Nevertheless, the risks do not seem to be dampening companies' buoyant mood. Companies represented in this survey are highly optimistic about their ability both to bring new drug products to market (80%) and to develop a competitive strategy that positions them well over the next five years (65%).

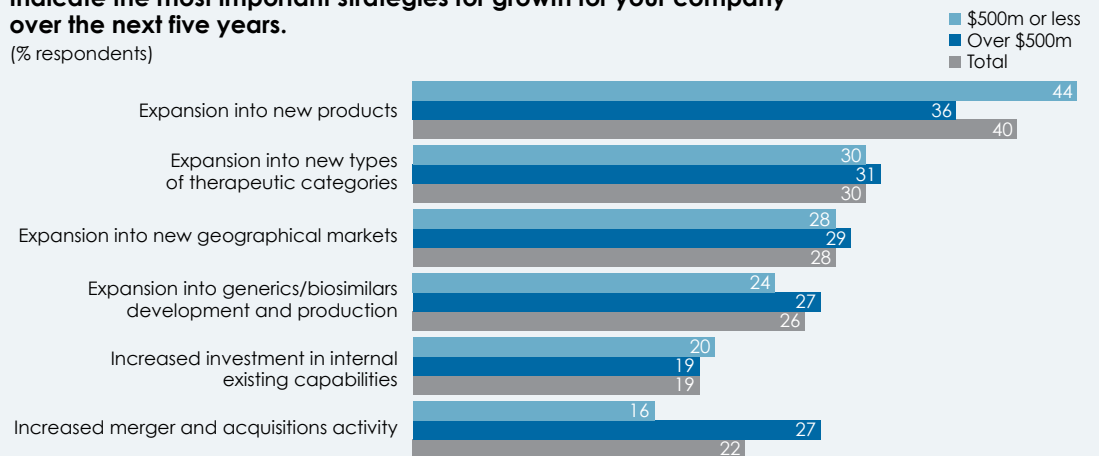
For Tom Ransohoff, vice-president and principal consultant at BioProcess Technology Consultants, this optimism makes sense. "You can't work in this industry and not be overwhelmed by the incredible advances in science and seeing this translated into real products," he says.

1 Growth strategies

Regardless of their company's size, survey respondents overwhelmingly indicate expansion into new products, expansion into new types of therapeutic categories and expansion within existing and into new geographic markets are their top strategic goals for growth for the next five years.

Indicate the most important strategies for growth for your company over the next five years.

(% respondents)



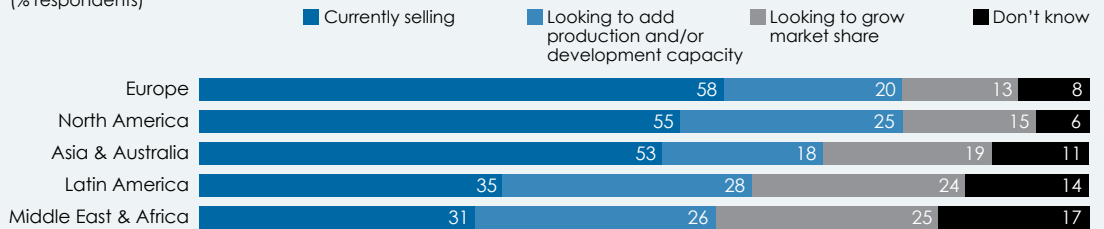
Source: Economist Intelligence Unit survey, 2016

Geographic growth

The survey finds that pharmaceutical companies are looking to expand their regional footprint over the next five years across the globe, with higher shares focused on adding capacity or market share in emerging markets.

Indicate your company's current operational status in each of the regions below and the status you expect over the next five years.

Select one in each row.
(% respondents)



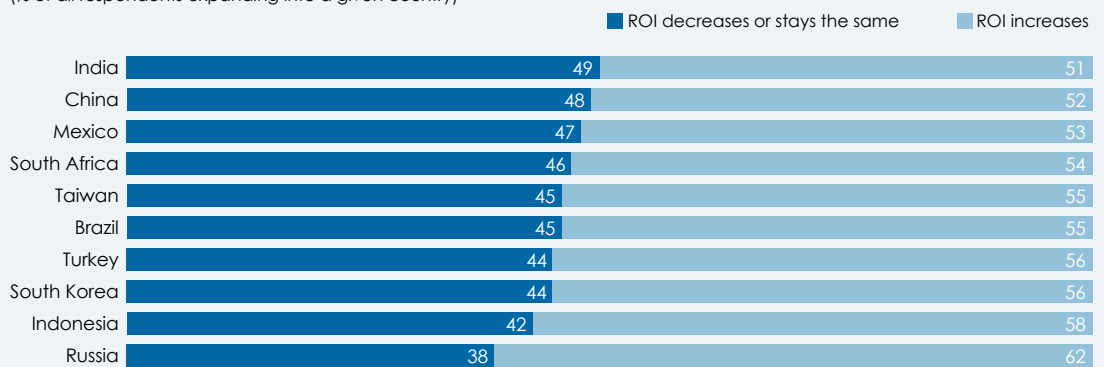
Source: Economist Intelligence Unit survey, 2016

This focus is notable given emerging markets' somewhat rocky overall economic performance. Asia came up as a particularly attractive region for the pharmaceutical sector in the next five years, with higher shares saying that they expect to be operating in many countries five years from now than say that they have current operations there: Indonesia (34% currently operating v 40% anticipate operating), South Korea (34% v 44%) and Taiwan (30% v 42%). Healthcare expenditure by household is also forecast to increase from 2015 levels in these three Asian markets by 75%, 37% and 12%, respectively, by 2020.¹

Indeed, the survey found high levels of optimism for emerging markets' potential overall. For every emerging market that respondents say they anticipate entering in the next five years, at least half of respondents also say that they anticipate return on investment (ROI) associated with entering emerging markets to increase in the next five years.

For each of the emerging markets, indicate which your company anticipates entering for any purpose in the next five years, and how, if at all, the company's return on investment (ROI) is expected to change for "entering emerging markets".

(% of all respondents expanding into a given country)



Source: Economist Intelligence Unit survey, 2016

¹ Economist Intelligence Unit, Consumer healthcare expenditure data, 2016

Product growth

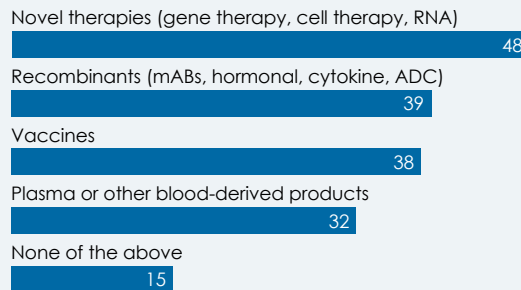
In terms of new therapies, “strides are being made in rare diseases and orphan drugs, rare diseases and autoimmune disease”, says Mr Baum. “And with Immuno-Oncology, you have a growing number of drugs with known efficacy in multiple indications.” These developments are quickly translating into profits. Sales of biologic products—which employ sophisticated bioprocessing technologies in their manufacture and are used to treat a host of chronic diseases including cancers, diabetes and arthritis—are rising sharply, expected to grow from a \$162bn market in 2014 to \$278bn by 2020.²

Many of the new therapies help to address conditions that previously had no significantly effective treatments; the demand for such biopharmaceuticals has been so insistent that these new drug therapies have received significantly more US FDA approvals in the 2015 calendar year than the average number approved annually over the last decade. It is not surprising, then, that biologics are a rising priority for most pharmaceutical companies surveyed.³

Indeed, the survey shows that stem cell-derived therapies and gene therapies top the list of drug categories deemed likely to disrupt short- and long-term corporate strategies. However, nearly half (48%) of survey respondents indicated that they themselves are considering or are already in the process of developing novel therapies; these newer therapies are taking a greater share of production focus than more traditional drug products such as vaccines (38%) and blood-derived products (32%).

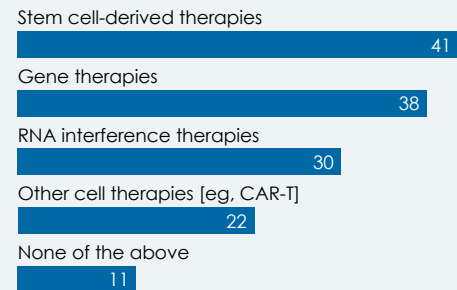
Indicate if your company is considering or already developing any of the following types of new drug products?

(% of all respondents)



Indicate which of the following novel therapy categories, if any, you expect to be disruptive enough to cause a change in your company's strategy whether you are considering developing them or not?

(% of all respondents)



Source: Economist Intelligence Unit survey, 2016

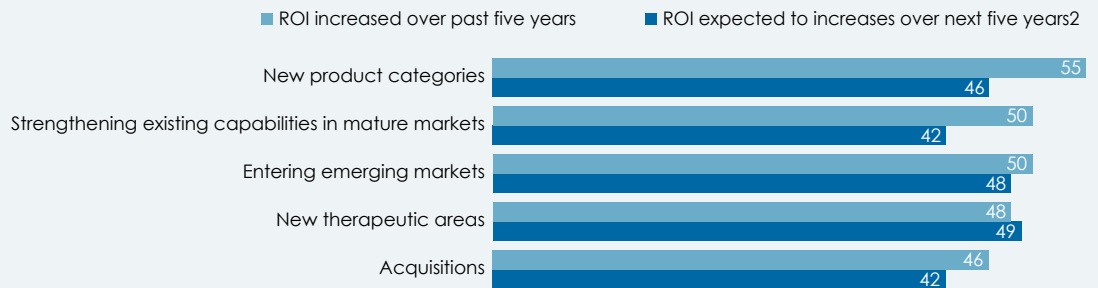
2 Persistence Market Research, Global Market Study on Biopharmaceuticals: Asia to Witness Highest Growth by 2020, <http://www.persistencemarketresearch.com/market-research/biopharmaceutical-market.asp>

3 U.S. Food and Drug Administration Center of Drug Evaluation and Research, Novel drugs 2015 summary, <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM485053.pdf>

Despite the perceived competitive threat, the survey further indicates that investment in the newest products has been and will continue to be profitable: Roughly half (48%) of respondents say they believe investments in new therapies performed better than their company's overall return on invested capital over the past five years. A similar percentage (49%) expect ROI to increase in these areas over the next five years.

Thinking about your company's investments in growth over the past five years, indicate how return on investment (ROI) has changed in the following areas. Furthermore, how do you expect ROI to change in these areas over the next five years?

(% of all respondents who said ROI was or is expected to be higher in these categories)



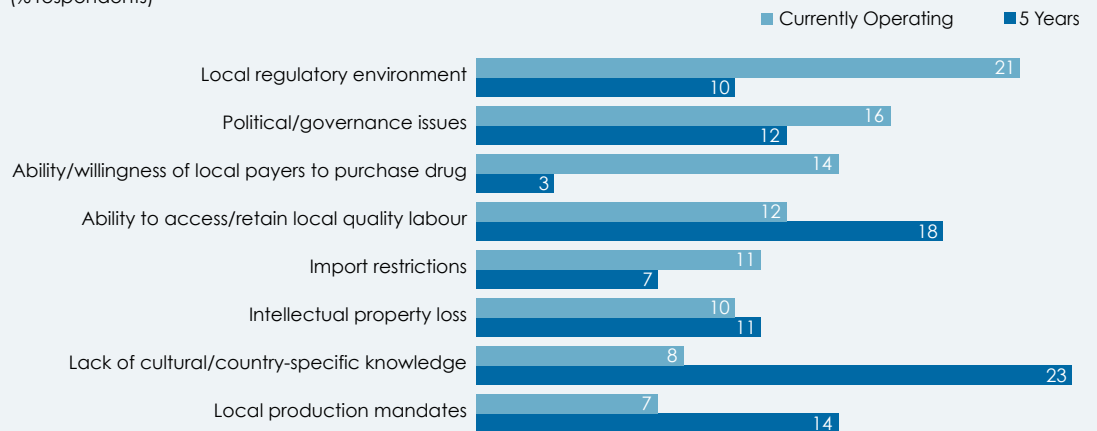
Source: Economist Intelligence Unit survey, 2016

2 Geographic risks

Pharma companies have been operating to some degree in many countries for decades. The geography-related risks they see now to their favoured growth strategies and those they expect to be the most important five years from now largely include regulatory and political concerns. Respondents also expect to be facing more cultural and labour issues five years from now.

In all of the countries where you are currently operating, indicate which risks are most important now versus in countries you expect to be operating in in five years.

(% respondents)



Source: Economist Intelligence Unit survey, 2016

A global range of regulations

Among emerging countries respondents most often indicate they are currently operating in Brazil, China and India—all are nations with somewhat risky regulatory environments that involve various levels of complicated mandates. In China, for example, Ralph Marcello, principal, Deloitte Consulting's life sciences consulting practice, sees a shift away from investment as a result of increased compliance risk, regulatory issues and price pressure on the Chinese national drug formulary (the list of medicines approved for prescription throughout the country).

"Some of our clients think it's too risky to have operations there now," says Mr Marcello,

who adds that he is seeing "significant investment into Singapore to serve the Southeast Asia region and, from there, to serve China". However, loss of intellectual property rights in China is less of a headache than it was previously, adds Mr Baum, who says China's has expressed willingness to clamp down on intellectual property theft as part of its efforts to encourage foreign investment. Across the countries in which they're operating today, only 10% of survey respondents see it as an important risk now, and that share barely budges, going only to 11%, looking five years ahead.

It's not just existing regulations that can be risky for companies expanding geographically, however—there's also the risk of regulations being changed. A full third of respondents highlight regulatory uncertainty as potentially disruptive to their company's strategy over the next five years. Adding the manufacture of new classes of untested biologic therapies in countries with unfamiliar or changeable regulations presents a high hurdle for companies considering that form of expansion.

But there is reason to be optimistic. Many emerging markets are standardising their pharmaceutical regulations and, in some cases, aligning them with global standards.

Mr Bates adds that there may be some hope for smoother regulatory paths going forward. For example, he points to the Transatlantic Trade and Investment Partnership, a proposed trade agreement between the US and the European Union. As it relates to the pharmaceuticals sector, the deal could allow for mutual recognition of data sets by US and European regulators. "That has the potential to de-risk and take some costs and time out of the regulatory process," he says.

Overall, in fact, respondents indicate that they are confident that they can fairly easily navigate regulatory regimes when getting their drugs approved—in both developed (62%) and emerging markets (45%).

Building local knowledge

Because multinational pharma companies have been managing operations in different cultures for decades as they've expanded geographically it's notable that this is the category of risk more executives expect to be creating concern five years from now than any other. Survey respondents cited several future risks associated with operating in new markets, such as lack of cultural knowledge, access to labour and meeting local production mandates. Companies will likely need to call on proven tools for managing different cultures, including hiring local employees at all levels, building relationships with governments and NGOs and contributing to civil society.

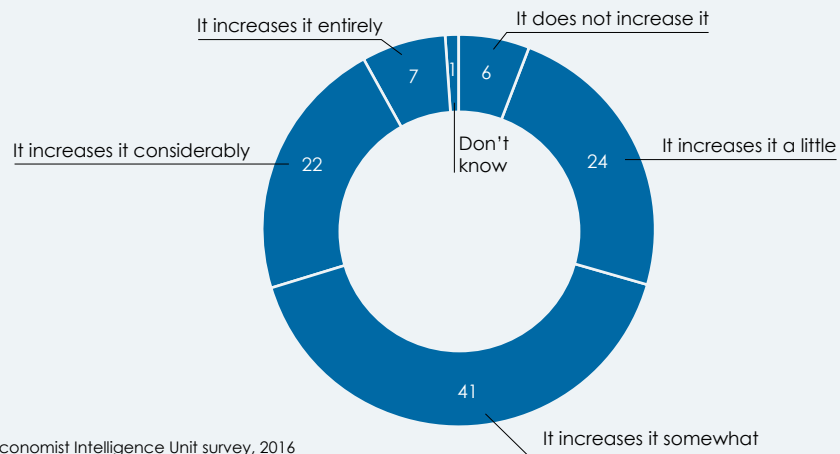
3 Product development risks

As has always been the case in the pharma industry, however, the geographic risks may pale next to the risks of developing entirely new types of drugs—whether companies are doing so themselves or facing competitors who are. Since survey respondents highlight cell therapies as the category most likely to disrupt corporate strategy, it follows that the majority (94%) of respondents see the development of new and different drug products as increasing the importance of risk management.

A majority (70%) believe that new products will increase the importance of risk management “somewhat”, “considerably” or “entirely”. Those risks include new science and scarce funds for development and revenue.

Does developing new and different products increase the importance of risk management?

(% respondents)



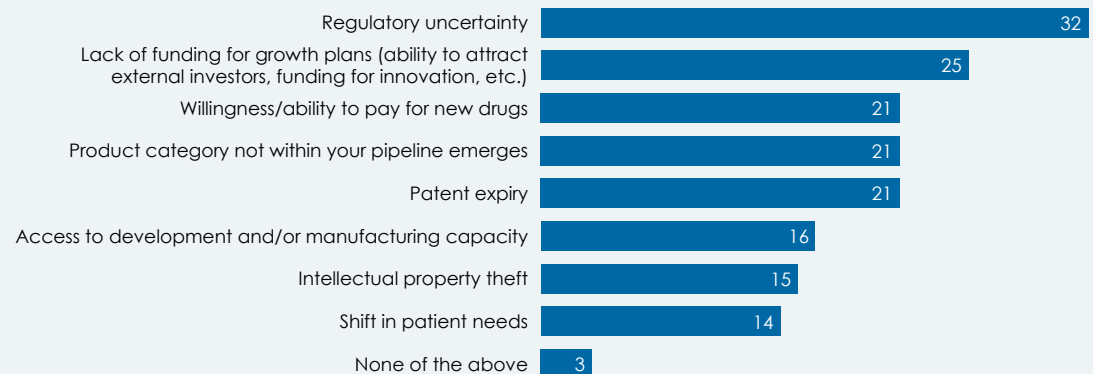
Source: Economist Intelligence Unit survey, 2016

Why funding matters so much

After regulatory uncertainty (32%), a lack of funding for growth emerged as the second-biggest concern (25%) for survey respondents overall.

Thinking about other types of risk that might disrupt your company's strategy over the next five years, which of the following, if any, most concern your company?

(% respondents)



Source: Economist Intelligence Unit survey, 2016

On the surface, this is somewhat surprising, as funding for the industry has been rising. For example, in the second quarter of 2015, overall investment by venture capitalists in the life sciences sector (biotechnology and medical devices combined) accounted for \$3.1bn, a 41% increase in dollars over the first quarter of 2015, according to an industry report by PwC.⁴

However, compared with more traditional therapies, production of novel cell and gene therapies is complex, expensive and difficult to replicate. "These [novel therapies] are really in the very earliest stages of clinical development," explains Mr Baum. "We don't know their long-term safety or efficacy." And beyond the funds poured into new developments efforts, which only occasionally pay off, the inherent complexity of manufacturing diverse types of biologics requires relatively more funding than traditional therapies.

However, Mr Bates notes excitement about and activity among UK companies in the potential of these therapies. "We're seeing significant reporting of pipelines being strong in this area and increased volumes of requests for scientific advice and classification for regulators," he says. "That's all activity that suggests there's quite a lot going on."

Novel therapies raise other questions, too. "How much do you invest in your current infrastructure and how much do you want to invest in these new emerging technologies and how much in older technologies like traditional small-molecule pharmaceuticals," asks Mr Ransohoff. "These are challenges that every company faces in terms of trying to allocate resources appropriately across the organisation."

⁴ PwC Pharmaceuticals and Life Sciences Industry Group, MoneyTree Life Sciences Report Quarterly Q2 2015 <http://www.pwc.com/us/en/health-industries/publications/assets/pwc-moneytree-life-sciences-funding-reaches-q2-2015.pdf>

Willingness to pay

Companies are concerned that funds may be scarce in another way, too—getting paid for new drug products, in particular novel therapies. Though the geographic data highlights that fewer companies are expecting ability to pay to be a major risk in the markets where they're operating five years from now, overall 21% are concerned at some level. "There's still some development in commercial viability that's required," says Mr Marcello. "The reality is that it's probably going to take a few more years before that technology matures in a way that we can see significant evidence of efficacy in the marketplace through these types of therapies."

Complicating the funding equation for new drugs and novel therapies are the headline debates over drug pricing in general, which are at their most intense in the US, where double-digit drug price rises have been the focus of congressional hearings. "Pricing is the major concern," says Mr Baum, "because that increases systemic risk and creates a lot of bad will—and creating bad will in a heavily regulated industry is not a good thing."

Patent expiration often not on the list

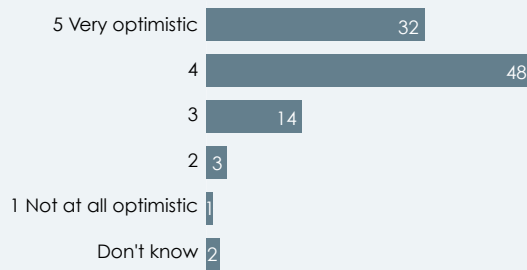
Pharmaceutical patent expiration—exposing top-selling drugs to competition from typically far less expensive generics—is hardly a new risk for the industry. And though it's persistent, only 21% of survey respondents cite it as one of the risks most likely to disrupt their strategy over the next five years.

4 Managing the risks to make strategy pay off

Despite these risks, pharmaceutical companies represented in this survey are largely optimistic about their ability to bring new drug products to market. They also express confidence in their ability to develop a competitive strategy over the next five years, a finding that is consistent regardless of company size.

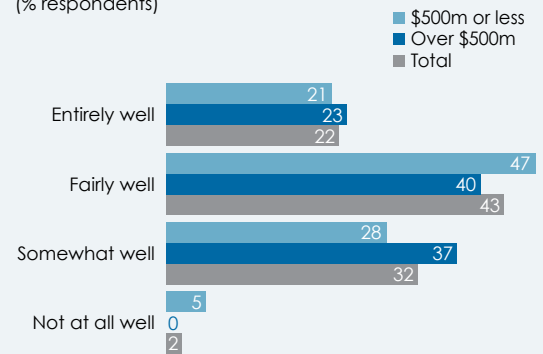
Indicate how optimistic are you overall about your company's ability to bring new drug products to market over the next five years?

(% respondents)



How does your company's overall strategy for developing and manufacturing new drug products position the company to compete over the next five years?

(% respondents)



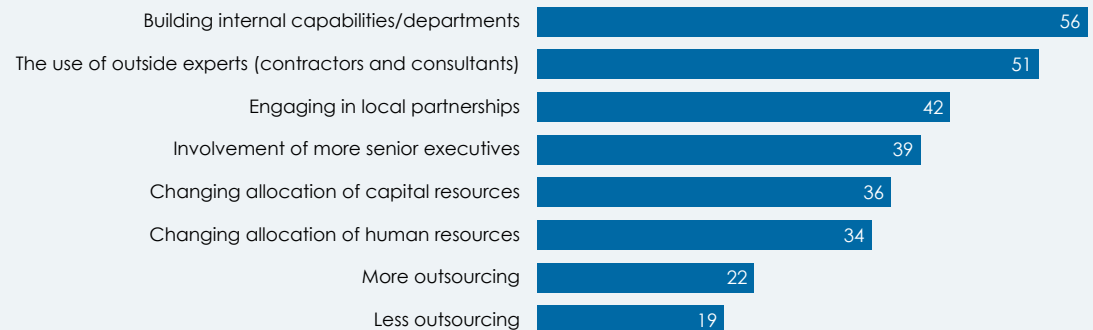
Source: Economist Intelligence Unit survey, 2016

In addition to the specific tactics cited above, to manage the risks which include regulatory, cultural, and funding risks, companies most often say they will be addressing them by building internal capabilities and collaborating with outside experts.

For most, the risk-management strategy will involve building internal capabilities and business units (56%), with the second-biggest group pointing to use of outside experts such as contractors and consultants (51%). As always, there are major trade-offs to consider in the decisions companies make about whether to focus on in-house resources or to look externally, as well as tasking internal resources to manage and take input from external partners. "There is now an appreciation of the challenges of working with an outsourcing provider in some areas," says Mr Bates. "And as money has got better in recent years, I'm seeing more companies choosing to do more in-house where they are able to, in part for control, in part for speed, in part for quality."

Indicate how your company manages the increased risk of developing new and different drug products?

(% respondents)



Source: Economist Intelligence Unit survey, 2016

Building relationships to thrive

In addition to straightforward outsourcing, a range of partnerships is also important to companies; forming local partnerships emerges as the third most popular strategy cited in the survey (42%).

“When it comes to product innovation we’re seeing a greater willingness to use open innovation, collaborations and partnership with smaller companies, academic institutions or mid-sized companies,” says Mr Marcello. “Companies recognise that the majority of innovation no longer comes from inside the walls of a large biopharma.” And sometimes the more novel the therapy, the more important it is to include a broad range of insights in the innovation process.

However, maintaining strong corporate partnerships can be tricky. Experts typically advise setting clear expectations, checking in on progress frequently and celebrating wins. In partnerships involving large amounts of intellectual property, reciprocity in sharing rewards is also increasingly held to be important.⁵

Matching strategy and risk management

Another important tactic the survey highlights is that companies appear to be managing risk differently depending on their strategies for developing new drug products. For example, 57% of survey respondents whose companies are investing in R&D centres in mature markets are reducing risk by building internal capabilities; only 41% of those companies are engaging in local partnerships to do so.

⁵ McKinsey & Company, Negotiating a better joint venture, <http://www.mckinsey.com/business-functions/strategy-and-corporate-finance/our-insights/negotiating-a-better-joint-venture>

PwC, Strategy+Business, Give-to-get corporate partnering <http://www.strategy-business.com/blog/Give-to-Get-Corporate-Partnering>



Conclusion

Pharmaceutical executives are, on the whole, bullish about the next five years. Most report that they have a balanced portfolio of growth plans and strong confidence that they can overcome the risks they expect to face. As Mr Baum noted, "in many ways, the industry has never had it so good."

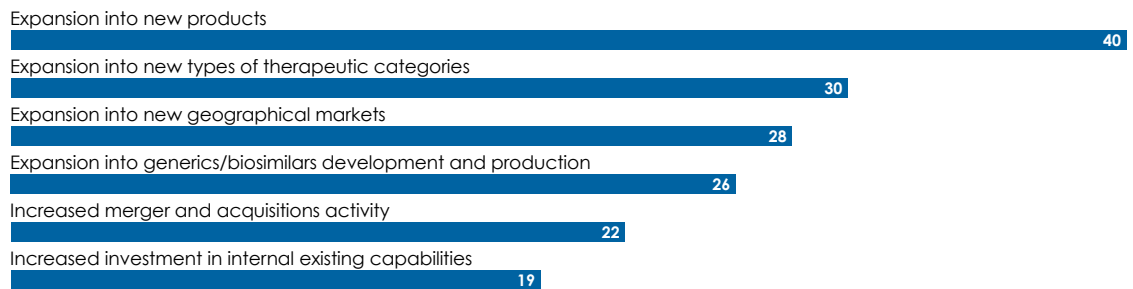
However, to earn the returns they expect, pharmaceutical companies will need to build their internal capabilities and manage a range of outsourcing and partner relationships. They will need to learn to thrive in new cultures and ensure that their geographic growth is diversified enough to prosper even if individual countries present economic or regulatory hurdles. And, as always, at the core they will need new science to succeed.

Appendix: survey results

Percentages may not add to 100% owing to rounding or the ability of respondents to choose multiple responses.

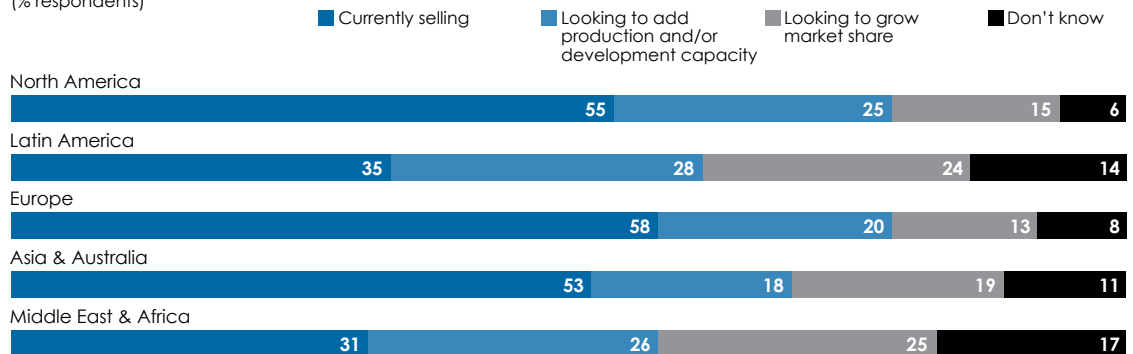
What are your company's most important strategies for growth over the next five years?

Please select up to two.
(% respondents)



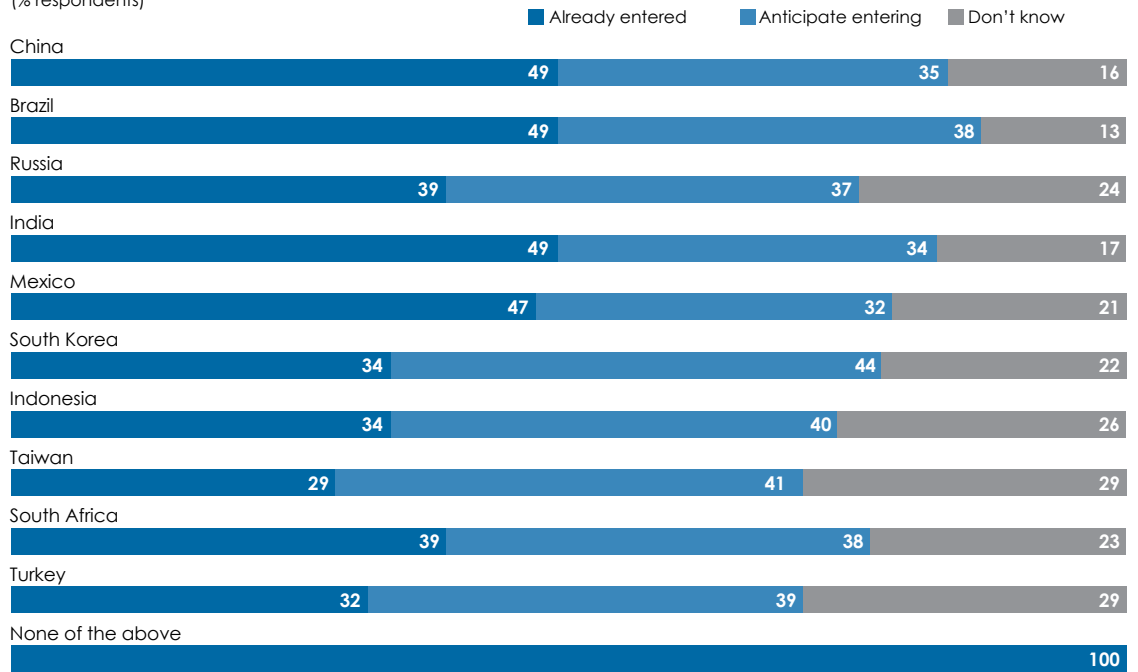
Indicate your company's current operational status in each of the regions below and the status you expect over the next five years.

Select one in each row.
(% respondents)



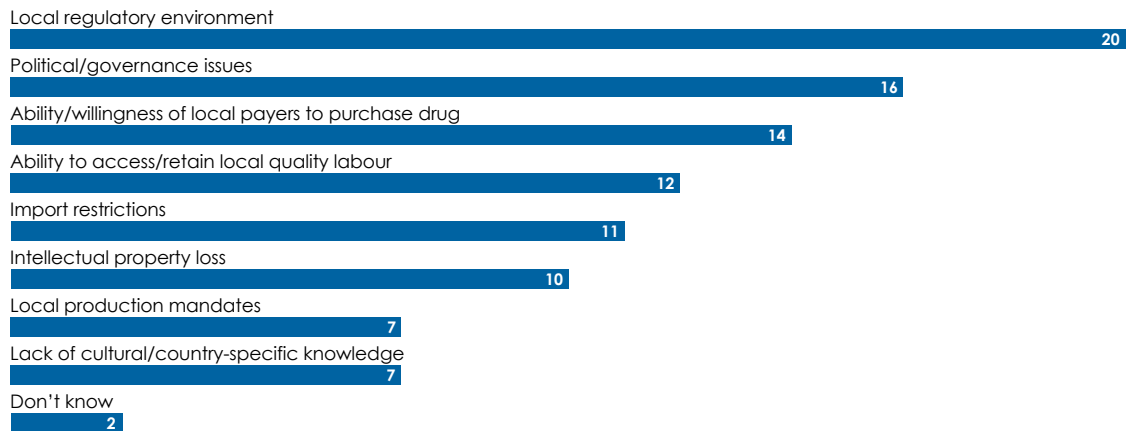
Which of the emerging country markets below, if any, have you entered for any purpose and which do you anticipate entering in the next five years?

Select one for each row.
(% respondents)



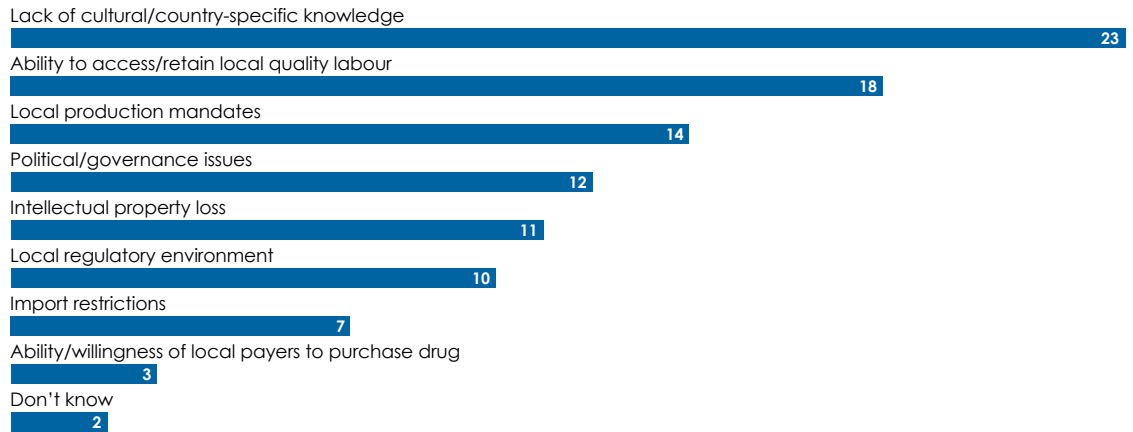
In all of the countries where you are currently operating, which of the risks below are most important now?

Select one.
(% respondents)



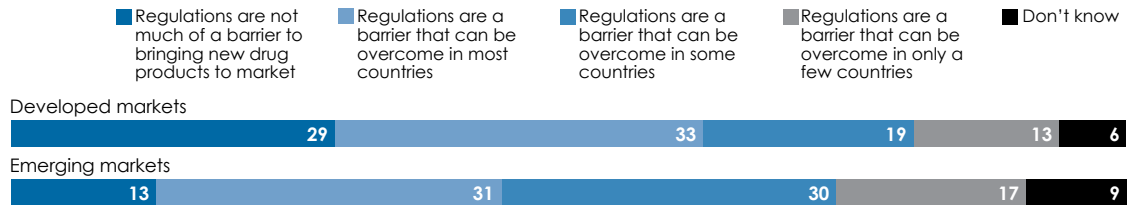
In all of the countries where you expect to be operating in five years, which of the risks below do you expect to be most important?

Select one.
(% respondents)



Which of the choices below, if any, best describe your company's views on current regulatory guidance for bringing new drug products to market?

Select one in each column.
(% respondents)



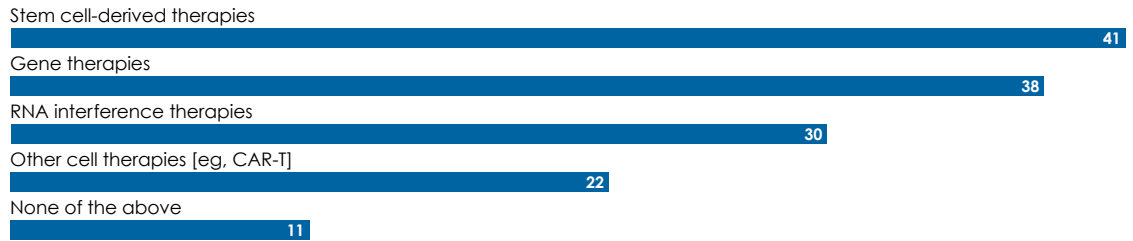
Are you considering or already developing any of the following types of new drug products?

Select all that apply.
(% respondents)



Which of the following novel therapy categories, if any, do you expect to be disruptive enough to cause a change in your company's strategy whether you are considering developing them or not?

Select up to two.
(% respondents)



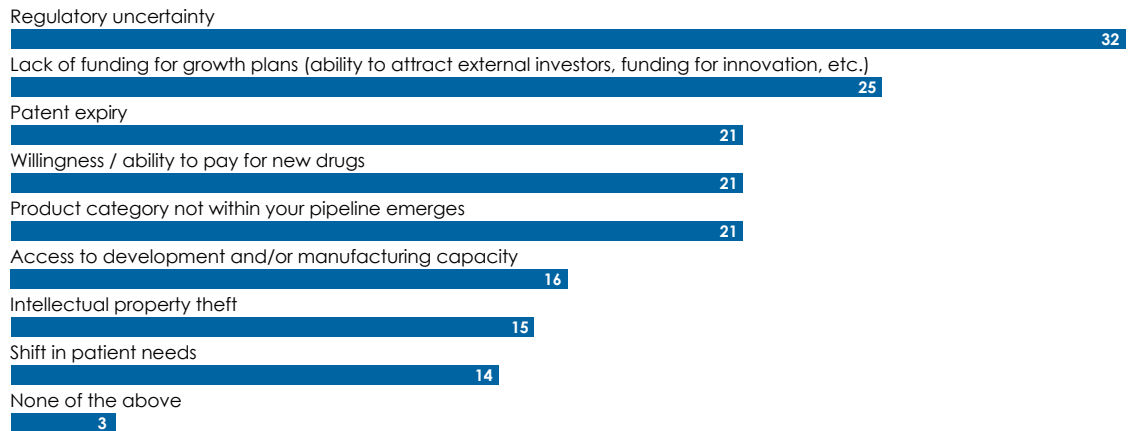
Thinking about novel therapy categories that might disrupt your company's strategy over the next five years, which types of competitors do you think will be the strongest players in these new product categories?

Select up to two.
(% respondents)



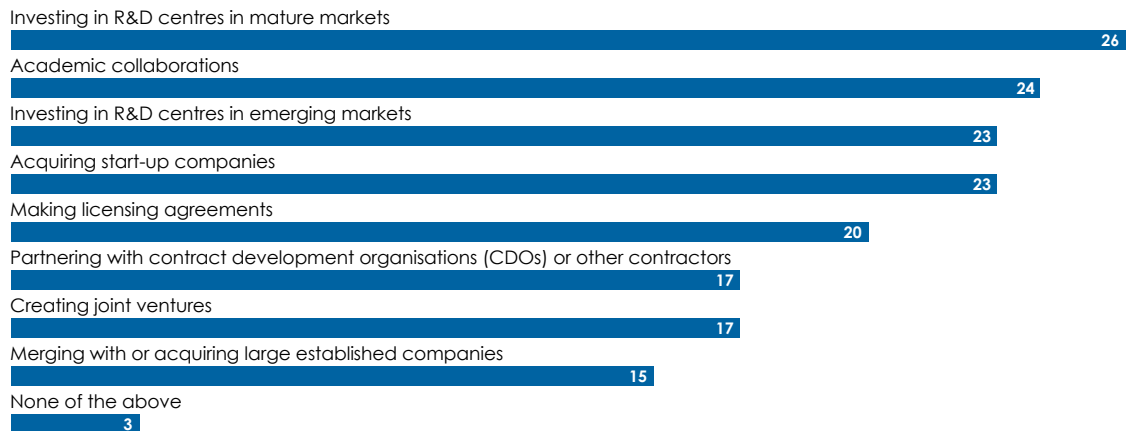
Thinking about other types of risks that might disrupt your company's strategy over the next five years, which of the following, if any, most concerns your company?

Select up to two.
(% respondents)



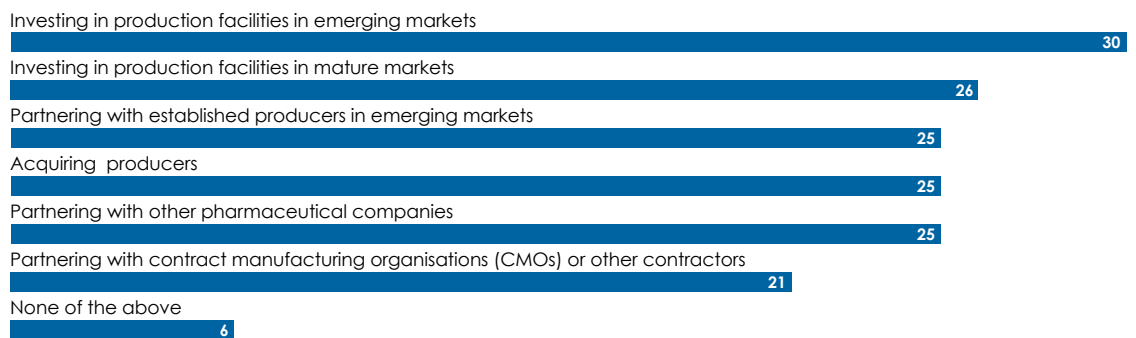
What are your company's main strategies for developing novel drug and therapy products?

Select up to two.
(% respondents)



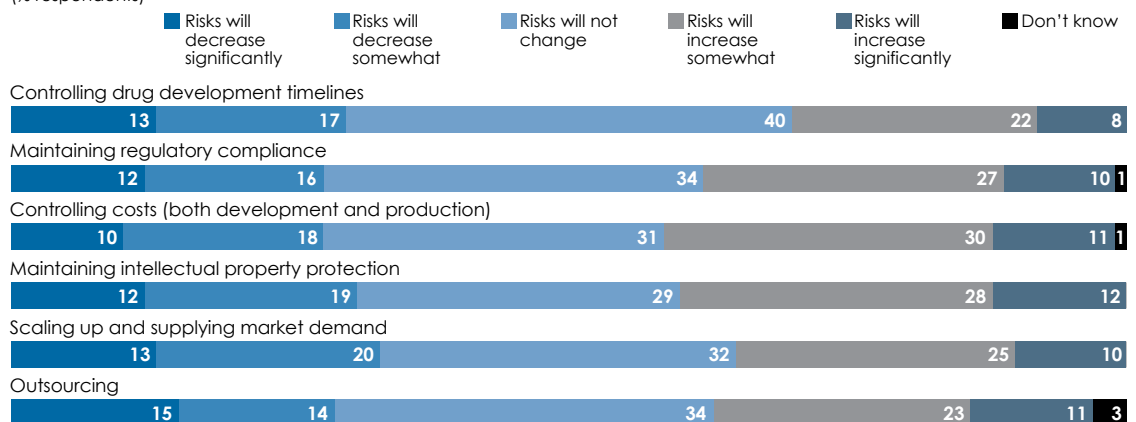
What are your company's main strategies for manufacturing new drug and therapy products?

Select up to two.
(% respondents)



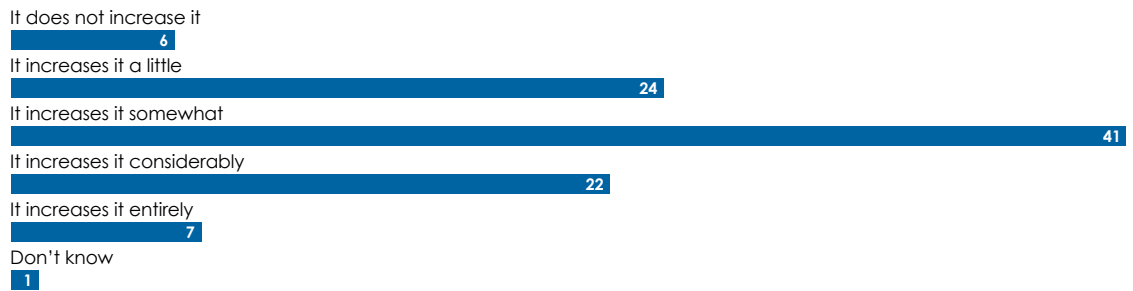
Over the next five years, as your company invests in the manufacture and development of new drug and therapy products, how might risks shift in each of the following areas?

Select one in each row.
(% respondents)



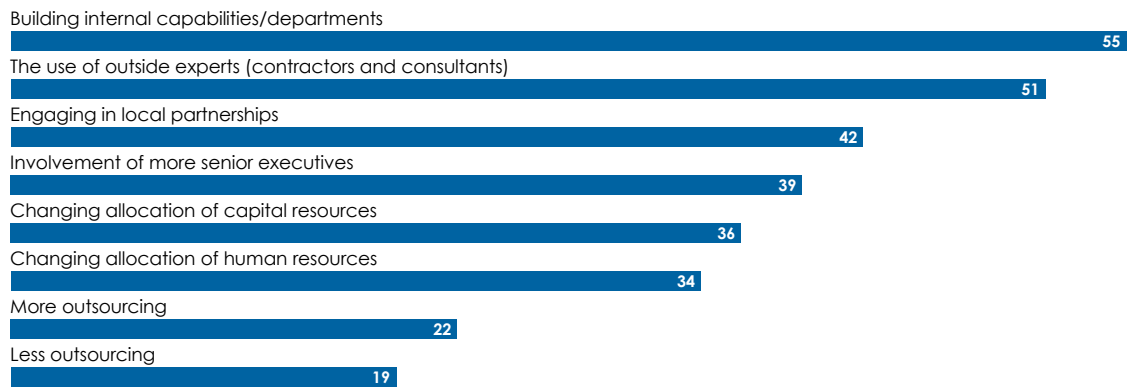
Does developing new and different drug products increase the importance of risk management?

Select one.
(% respondents)



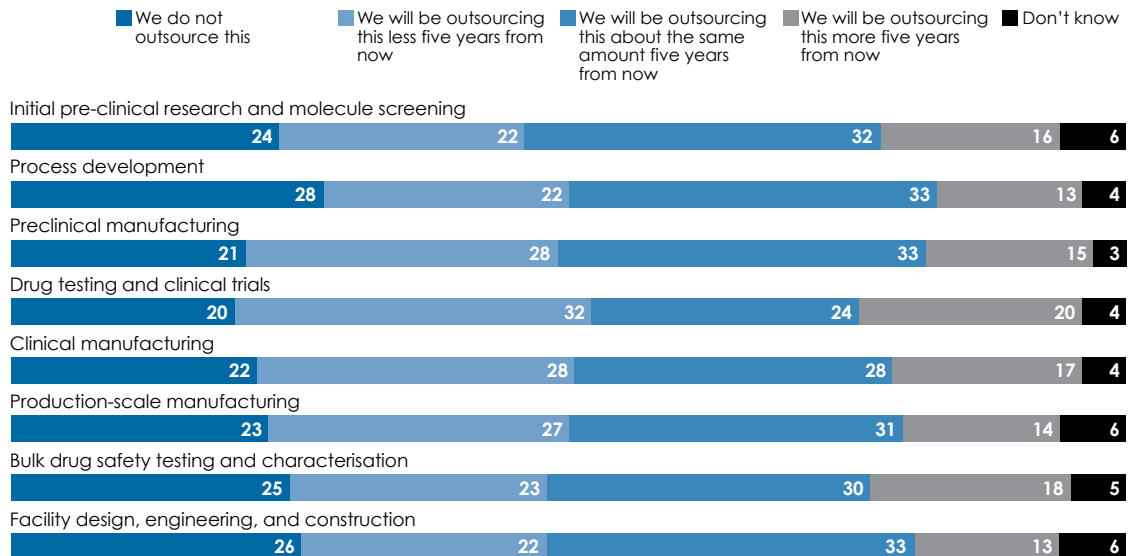
How do you manage the increased risks of developing new and different drug products?

Select up to three.
(% respondents)



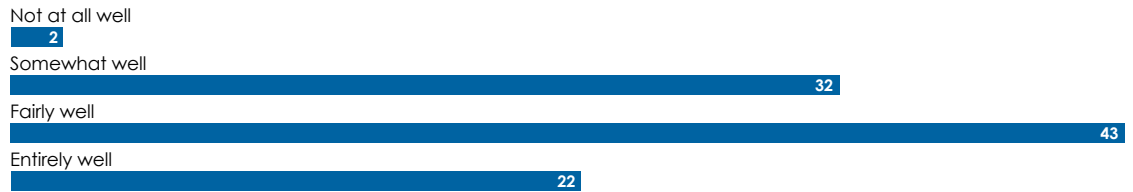
How, if at all, does your company plan to change the degree of outsourcing in each of the following specific areas of operation over the next five years?

Select one in each row.
(% respondents)



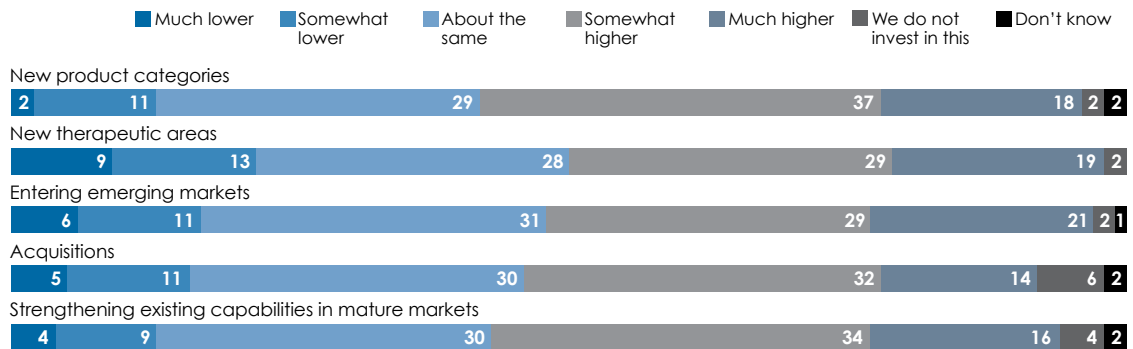
How does your company's overall strategy for developing and manufacturing new drug products position the company to compete over the next five years?

Select one.
(% respondents)



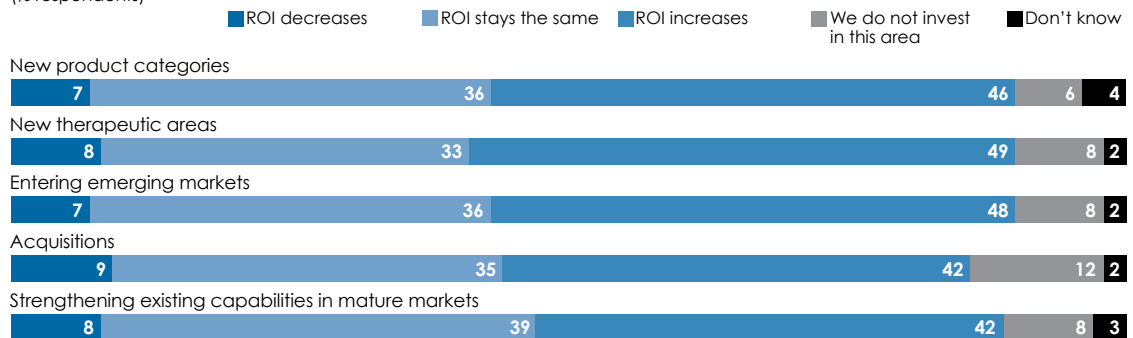
Thinking about your company's investments in growth over the past five years, how has your return on investment in each of the areas below compared with the company's overall return on invested capital?

Select one in each row.
(% respondents)



Over the next five years, how, if at all, do you expect your company's return on investment (ROI) in each area to change?

Select one in each row.
(% respondents)



How optimistic are you overall about your company's ability to bring new drug products to market over the next five years?

Select one.
(% respondents)



How does your company compare to its industry peers in terms of profitability?

Select one.
(% respondents)



Does your company currently partake or is it planning to partake in any biopharmaceuticals development, and are you familiar with strategy and operations in that area?

Select one.
(% respondents)

Yes, we are pursuing and I am familiar with the strategy and operations **89**

Yes, we are pursuing and I am not familiar with the strategy and operations **11**

No, we are not pursuing any biopharmaceutical development **0**

Don't know **0**

What are your organisation's global annual revenues in US dollars?

(% respondents)

\$500m or less **50**

\$500m to \$1bn **17**

\$1bn to \$5bn **20**

\$5bn to \$10bn **10**

\$10bn or more **4**

Which of the following most closely describes the work your organisation undertakes?

Select all that apply.
(% respondents)

Originator in R&D **51**

Originator in production **42**

Contract manufacturing **33**

Contract research and development **32**

Biosimilars **29**

Which of the following best describes your title?

Select one.
(% respondents)

Board member **5**

CEO/President **10**

COO or equivalent **16**

CFO or equivalent **8**

Other C-level executive **10**

SVP/VP/Director **50**

Which of the following best describes your function?

Select one.
(% respondents)

Business development **16**

Manufacturing **15**

Project management **15**

Commercial strategy **12**

Clinical research **9**

Strategic planning **8**

Marketing and sales **7**

Research and development **7**

Supply chain / procurement **4**

Quality **4**

Regulatory affairs **3**

Whilst every effort has been taken to verify the accuracy of this information, neither The Economist Intelligence Unit Ltd. nor the sponsor of this report can accept any responsibility or liability for reliance by any person on this report or any of the information, opinions or conclusions set out in the report.

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