Scrip Pharma intelligence

Rentschler Biopharma

LEUKOCARE BIOTECHNOLOGY

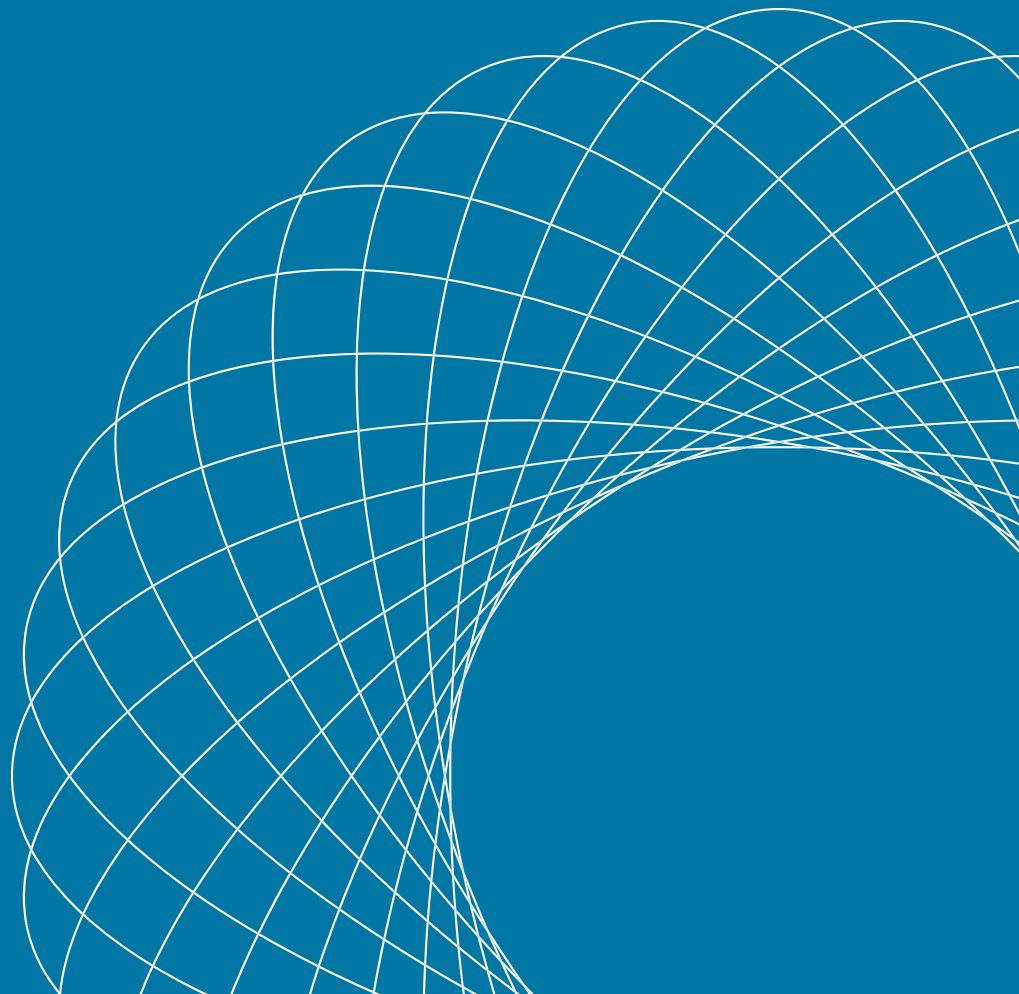
INDUSTRY INSIGHTS – 2018 SURVEY

Formulation in the Drug Development Process

informa engage
TARGETED MARKETING SERVICES

Table of Contents

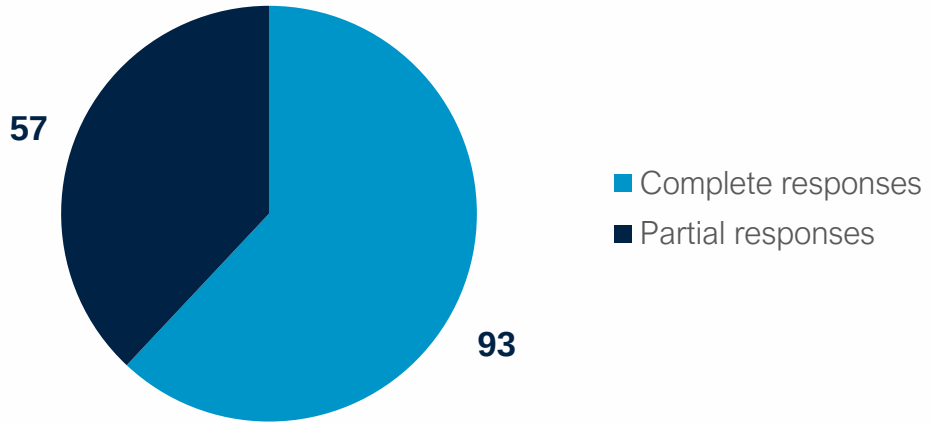
Executive Summary



Introduction and Overview

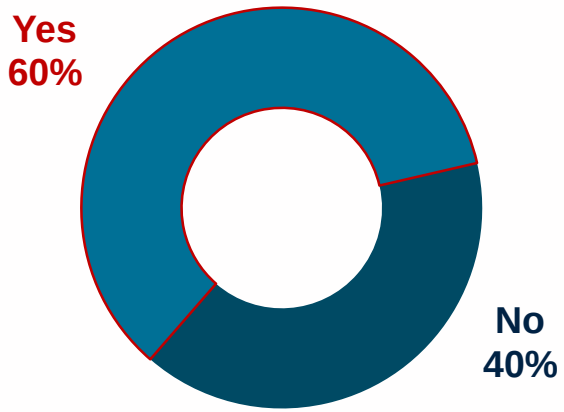
- Survey was conducted by Informa Engage on behalf of Informa Pharma Intelligence, Rentschler Biopharma SE and Leukocare AG
  - Purpose was to evaluate the status quo, importance and future of formulation in the drug product development process
  - Study methodology conforms to accepted marketing research methods, practices and procedures
  - Data were collected between July 23rd and September 4th, 2018

- Completion of Survey:
  - 150 qualified responses from participants active in the industries of biopharmaceuticals and/or vaccines
  - 93 were completed surveys and 57 were partial
  - A variety of job focuses are represented in the survey, with Clinical development and Drug product development being most common



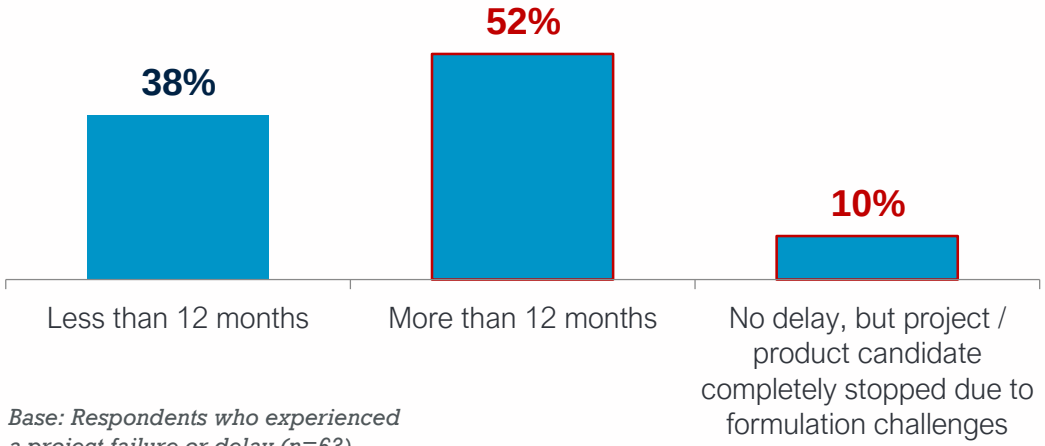
Project Failure or Delay Because of Formulation Challenges

Have you ever experienced a project failure or a significant delay, because of formulation challenges?



Base: All respondents (n=105).

How long was the project delayed because of the formulation challenges?

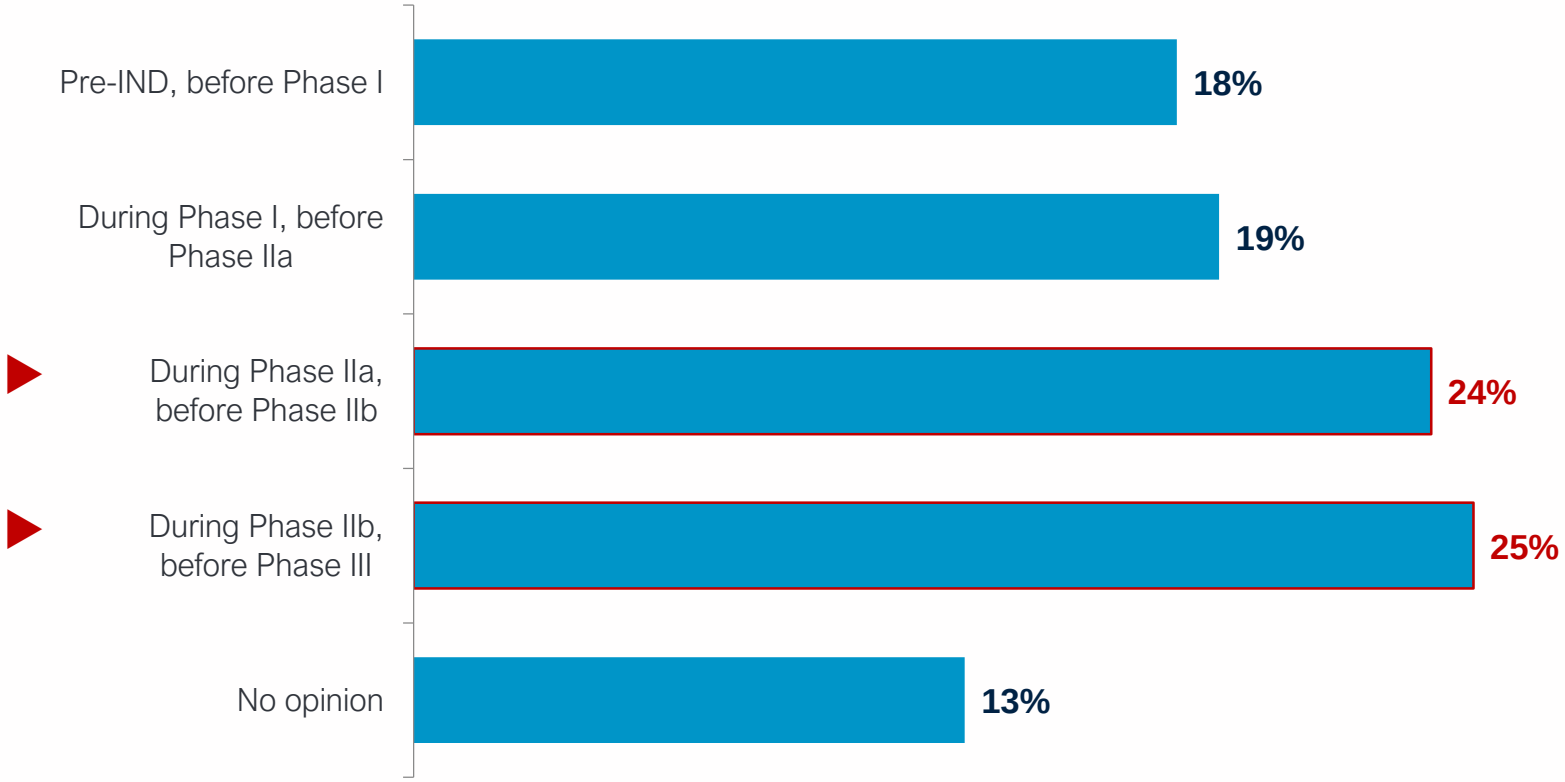


Base: Respondents who experienced a project failure or delay (n=63).

- Formulation issues have led to project failure and significant delays for about 60% of responding companies
- Of those projects, a delay of more than 12 months was reported by 52%
- 10% experienced complete failure
- This makes formulation a key opportunity in the process of drug development

The Perfect Moment to Deploy a 'Commercially Viable' Formulation

In which stage of the drug product development should a 'commercially viable' formulation be deployed?

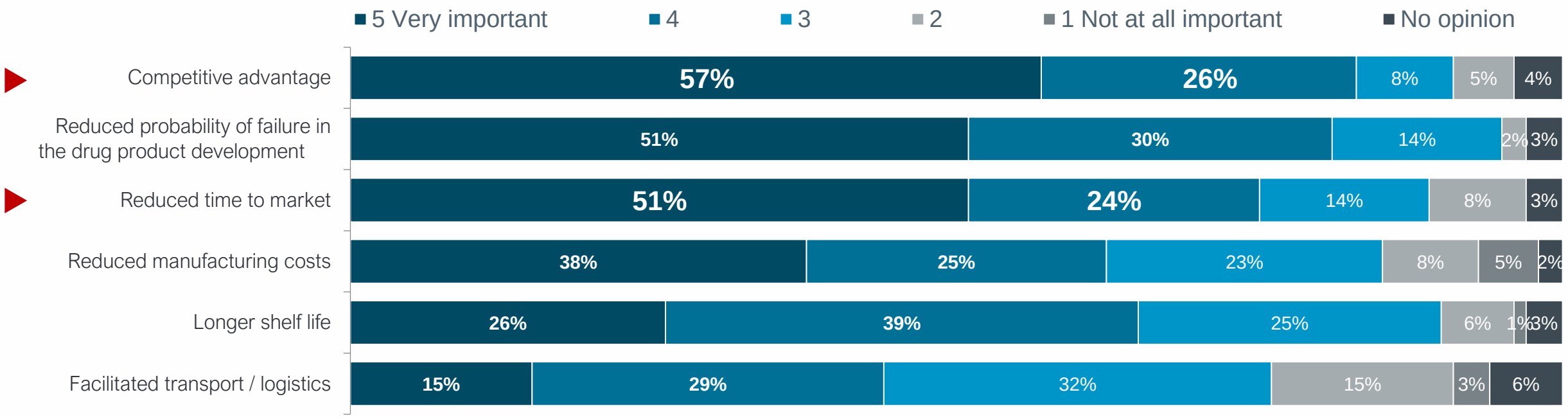


- About half the respondents specified that deployment of a 'commercially viable' formulation should take place between the stages
  'During Phase IIa before Phase IIb' and
  'During Phase IIb before Phase III'
- Only 18% start as early as 'Pre-IND, before Phase I'

Base: All respondents (n=150).

Important Decision Criteria in Formulation

On a scale from 1 to 5, please rate the importance of the following aspects of formulation:

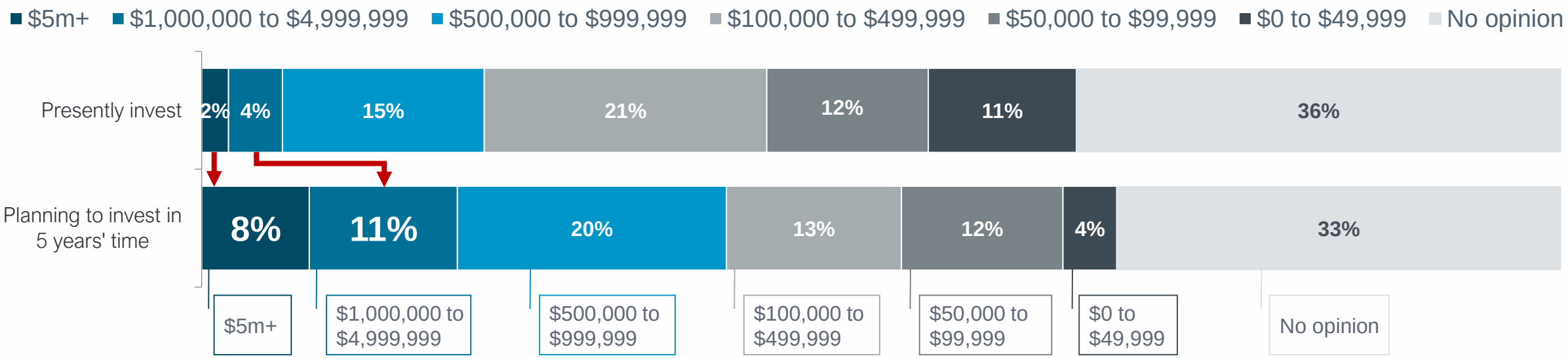


- 83% of respondents attributed ‘competitive advantage’ as ‘very important or important’
- 75% found a ‘reduced time to market’ ‘very important or important’
- What aspects of formulation can help leveraging additional business opportunities, and in which phase of development?

Base: All respondents (n=106). [1]Note: top-two box : 5 Very important & 4 scores.

Growing Investment in the Next 5 Years

Approximately how much does your organization invest in early stage formulation per project annually? (US$)

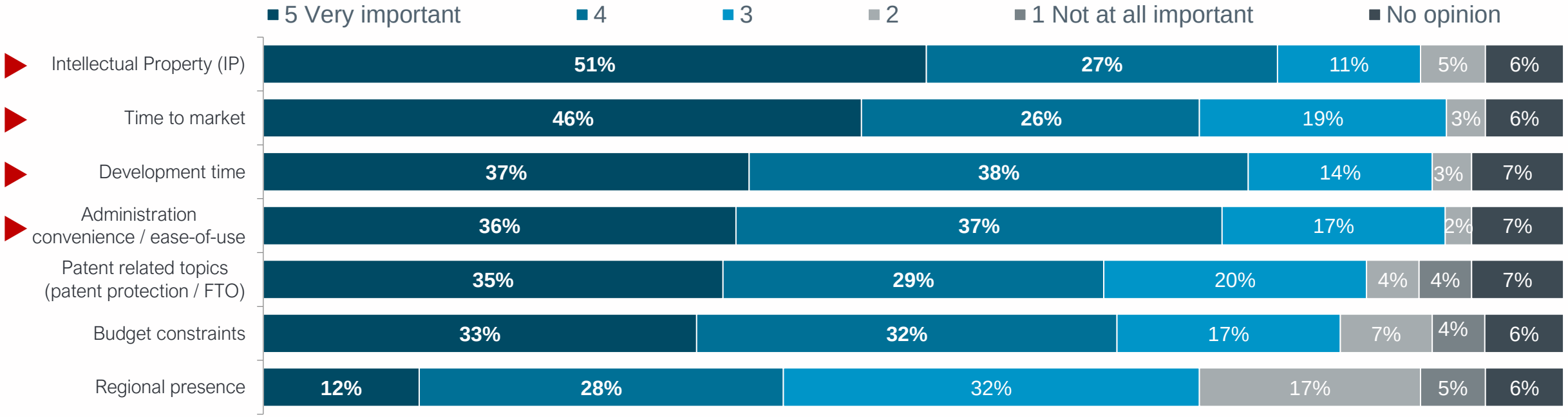


- Responses show willingness to invest more funds in early stage formulation within next 5 years
- Three times more companies plan to spend between US$ 1 million to US$ 5+ million per formulation project over next 5 years

Base: All respondents (n=95).

Important Considerations When Evaluating Formulation Strategy

How important are the following considerations when evaluating your formulation strategy?

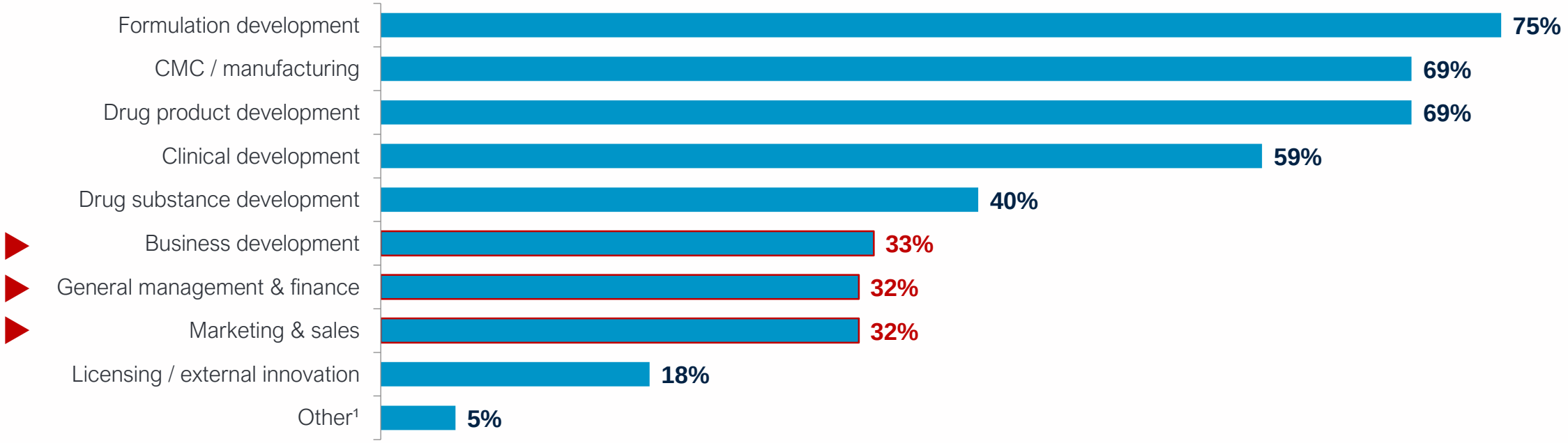


- Intellectual Property, development time and ease-of-use top list of formulation priorities
- Contradictory to relatively late decision on development of a 'commercially viable' formulation?
- Do commercial aspects need to be considered more when evaluating a formulation strategy?

Base: All respondents (n=94).

Departments Included in the Formulation Decision Making Process

Which departments are included in the formulation decision making process?



- Departments included in formulation decision making are: formulation, bioprocess, drug product and clinical specialists
- Commercialization departments seem to be involved to a much lesser extent
- Important role in planning commercial value and success of marketed products reflected?

Base: All respondents; multiple answers permitted (n=93).

[1]Other inc. Not Applicable since we are a research site and conduct clinical trials phase I, II, III and IV, Quality Assurance, Regulatory & Regulatory affairs.

Scrip Pharma intelligence

Rentschler Biopharma

LEUKOCARE BIOTECHNOLOGY

FULL REPORT – 2018 SURVEY

Formulation in the Drug Development Process

informa engage
TARGETED MARKETING SERVICES

Table of Contents

Table of Contents

Introduction & Methodology

OVERVIEW

Methodology, data collection and analysis by Informa Engage, on behalf of Pharma Intelligence, Rentschler SE and Leukocare AG Biotechnology.

Data collected between July 23rd and 4th September 2018.

Methodology conforms to accepted marketing research methods, practices and procedures.

METHODOLOGY

On July 23rd 2018, Pharma Intelligence emailed invitations to participate in an online survey to members of the Scrip database.

By September 4th 2018, Informa Engage had received 150 qualified responses, of which 93 were completed surveys, and 57 were partial response.

Only respondents who were active in the industries of biopharmaceuticals and/or vaccines qualified to participate.

RESPONSIVE MOTIVATION

To encourage prompt response and increase the response rate overall, a live link to the survey was included in the email invitation to route respondents directly to the online survey.

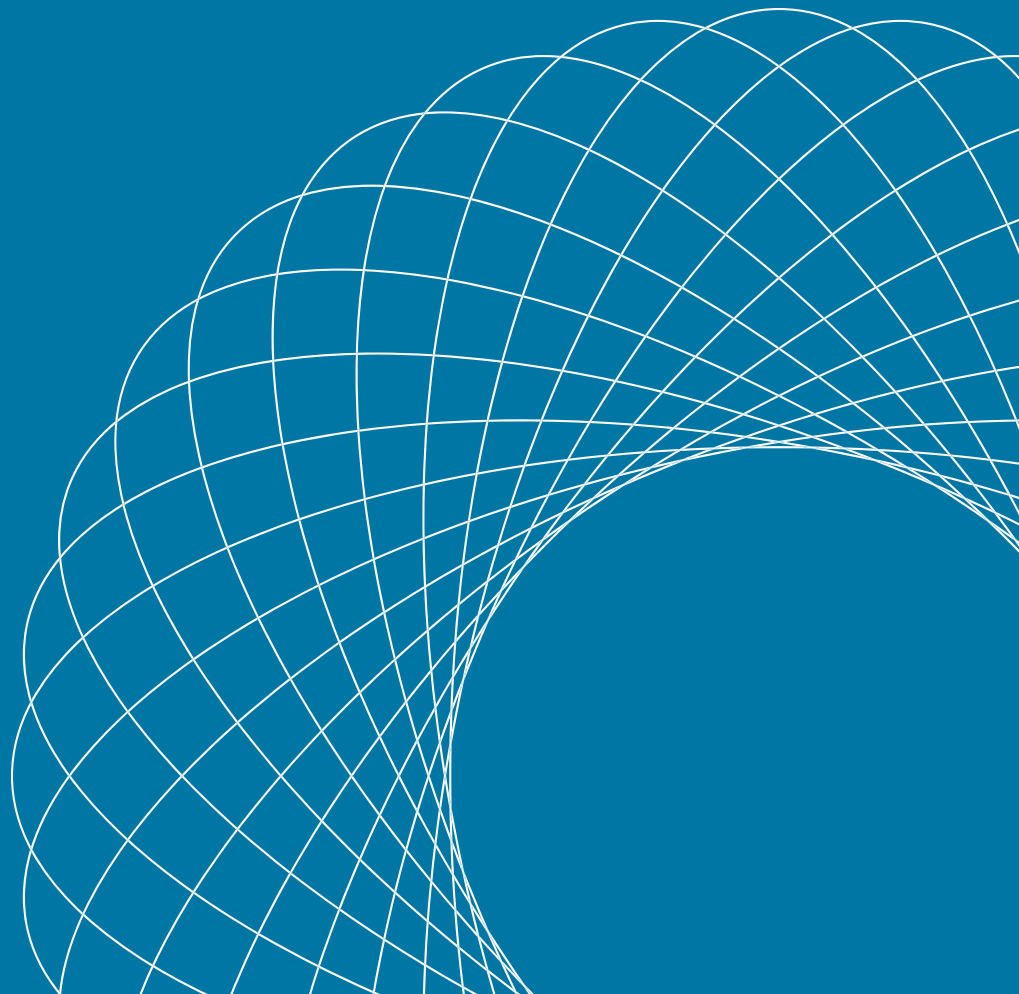
The invitations and survey were branded with the Pharma Intelligence, Rentschler SE and Leukocare AG names and logos, in an effort to capitalize on user affinity for this valued brand.

Each respondent (including non-qualified responses) was afforded the opportunity to enter a drawing for one of four €/$/£50 Visa gift cards.

The incentive was enhanced on the 23rd August, so that each qualified respondent (going forward) was afforded the opportunity to receive a €/$/£10 Amazon gift card.

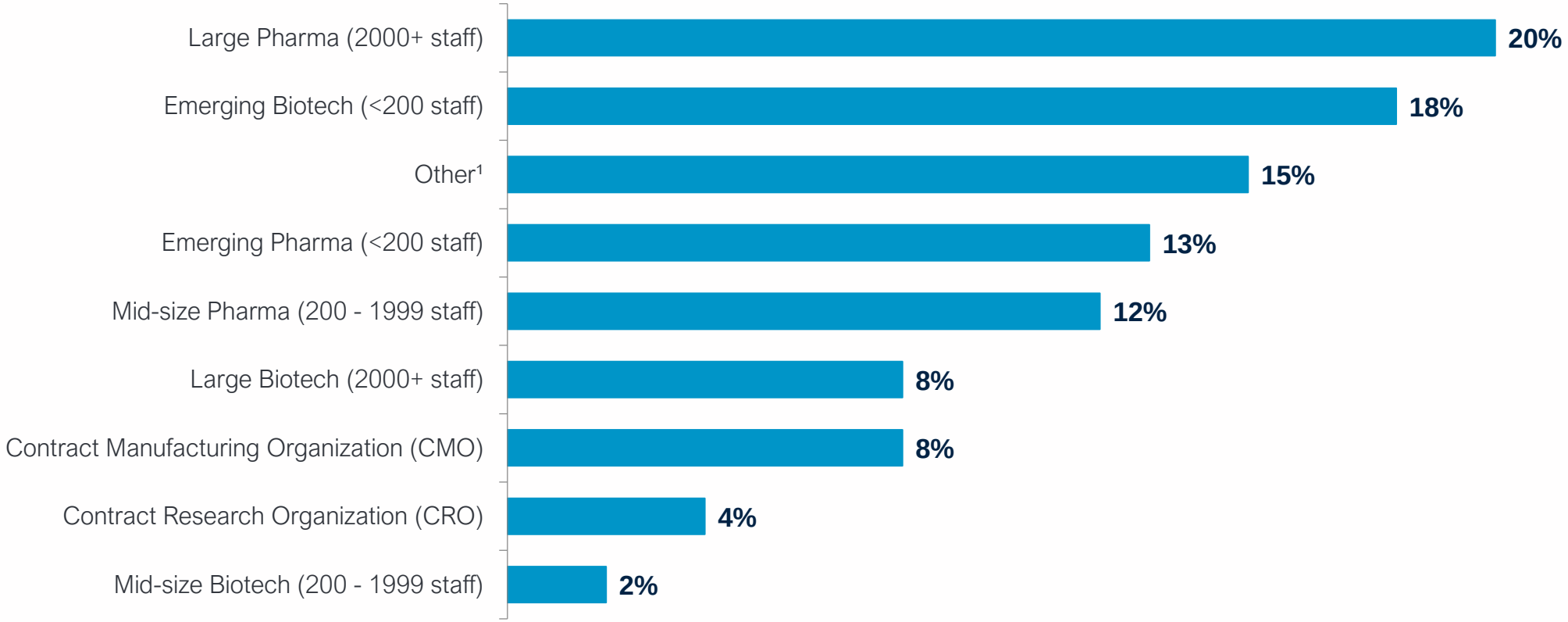
Follow-up emails were sent to non-respondents.

Respondent Profile



Company Type

What type of company do you currently work for?

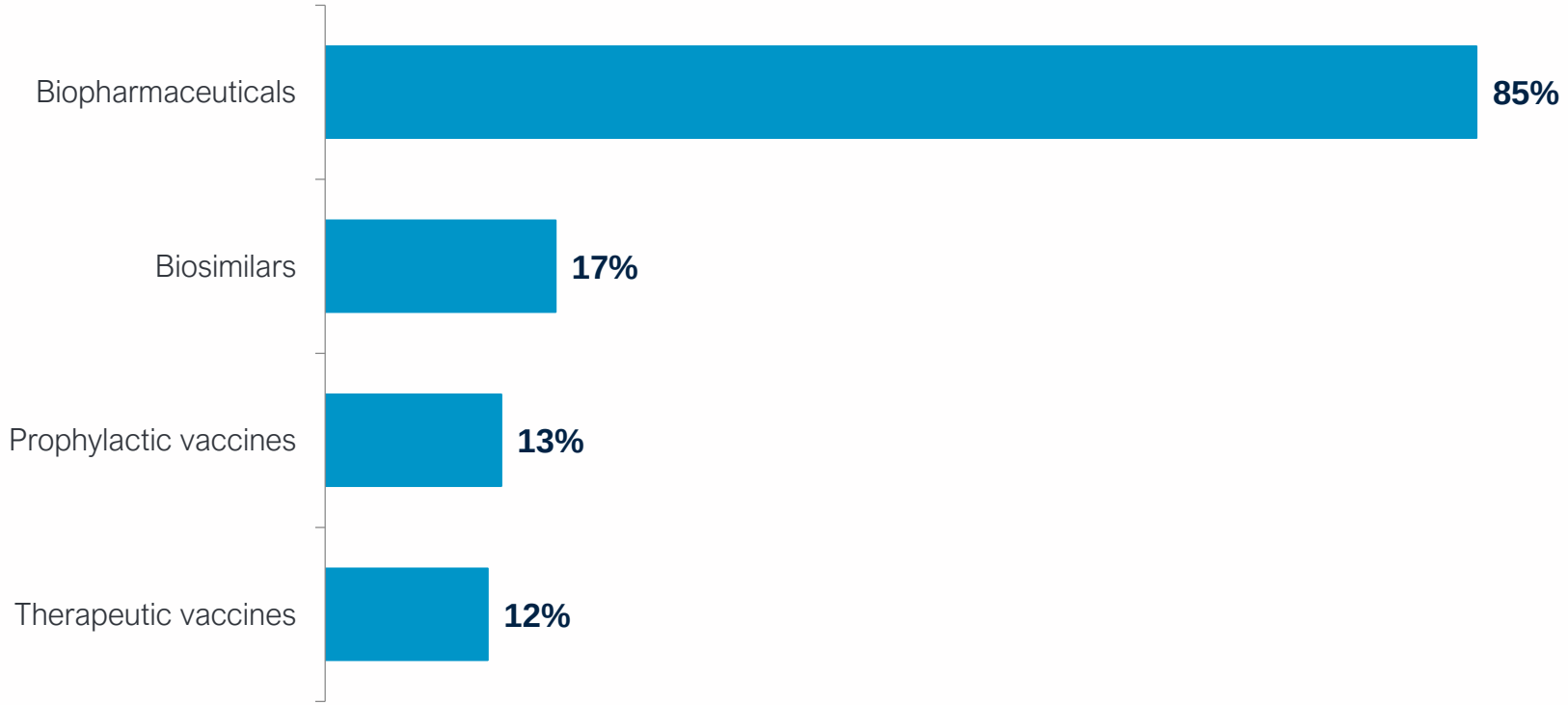


Base: All respondents (n=93).

[1]Other inc. Academia (x2), Virtual Biotech, Health System, Consultant (x3), Industry Association, MCO, R&D Non-profit & Multi-Speciality Research Site Network.

Company's Main Focus

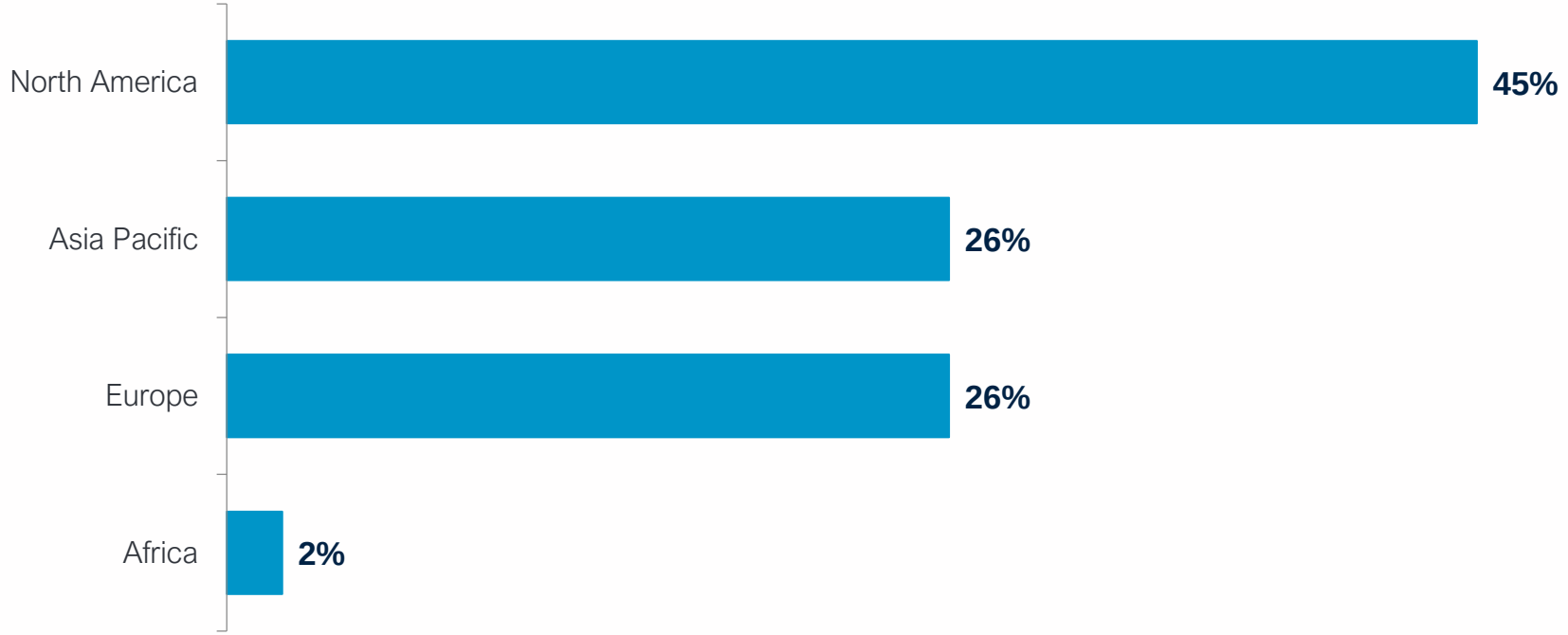
What is the main focus of your company?



Base: All respondents; multiple answers permitted (n=89).

Regional Location

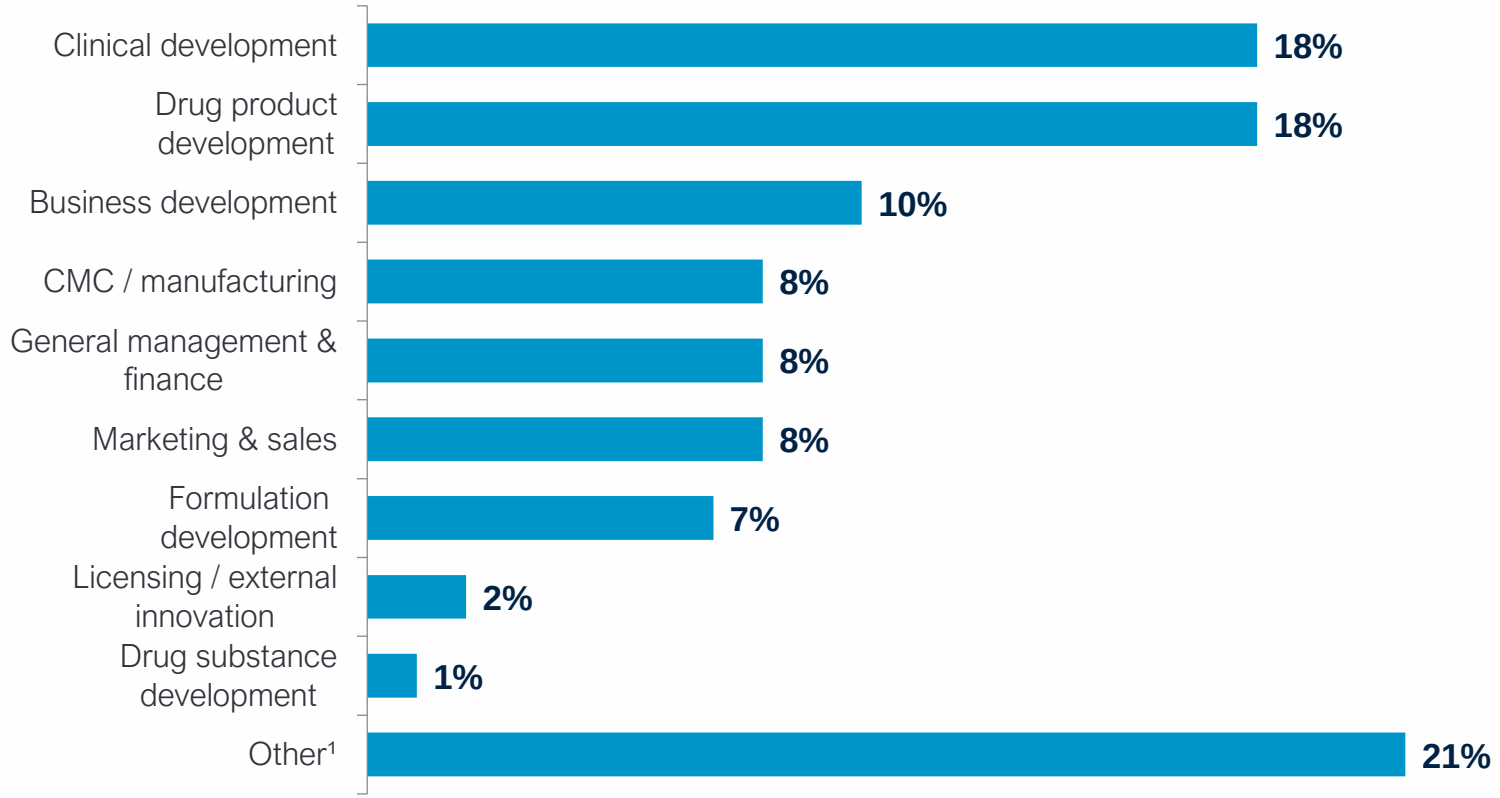
In which region are you primarily based?



Base: All respondents (n=91).

Job Function

Which of the following best describes your job function?



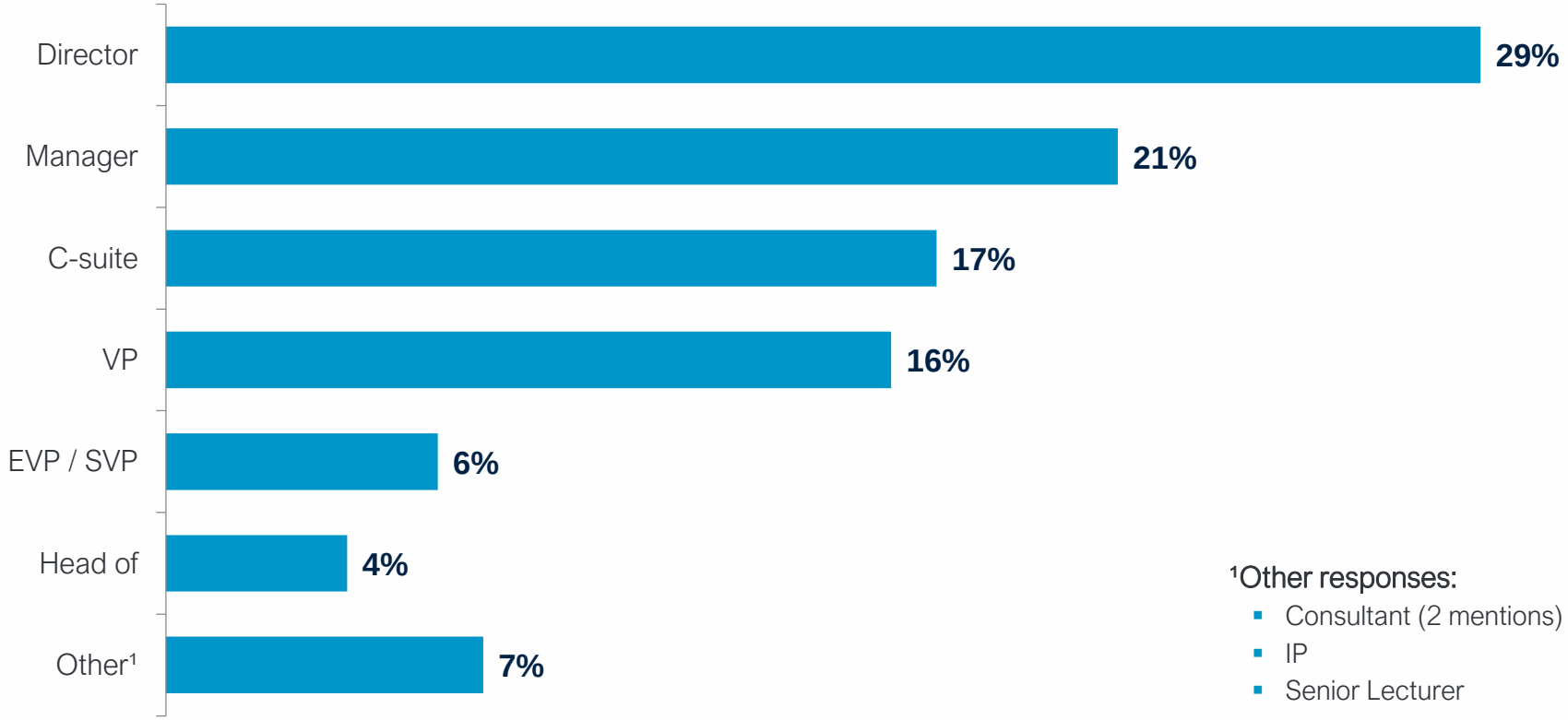
[1]Other responses:

- Academic
- C Suite (2 mentions)
- Clinical Management
- Consulting
- Healthcare Policy
- IP
- Medical department
- Preclinical leader
- Quality (2 mentions)
- R&D
- Regulatory - formerly CMC development
- Regulatory Affairs (2 mentions)

Base: All respondents (n=90).

Level of Seniority

Which of the following best describes your level of seniority?

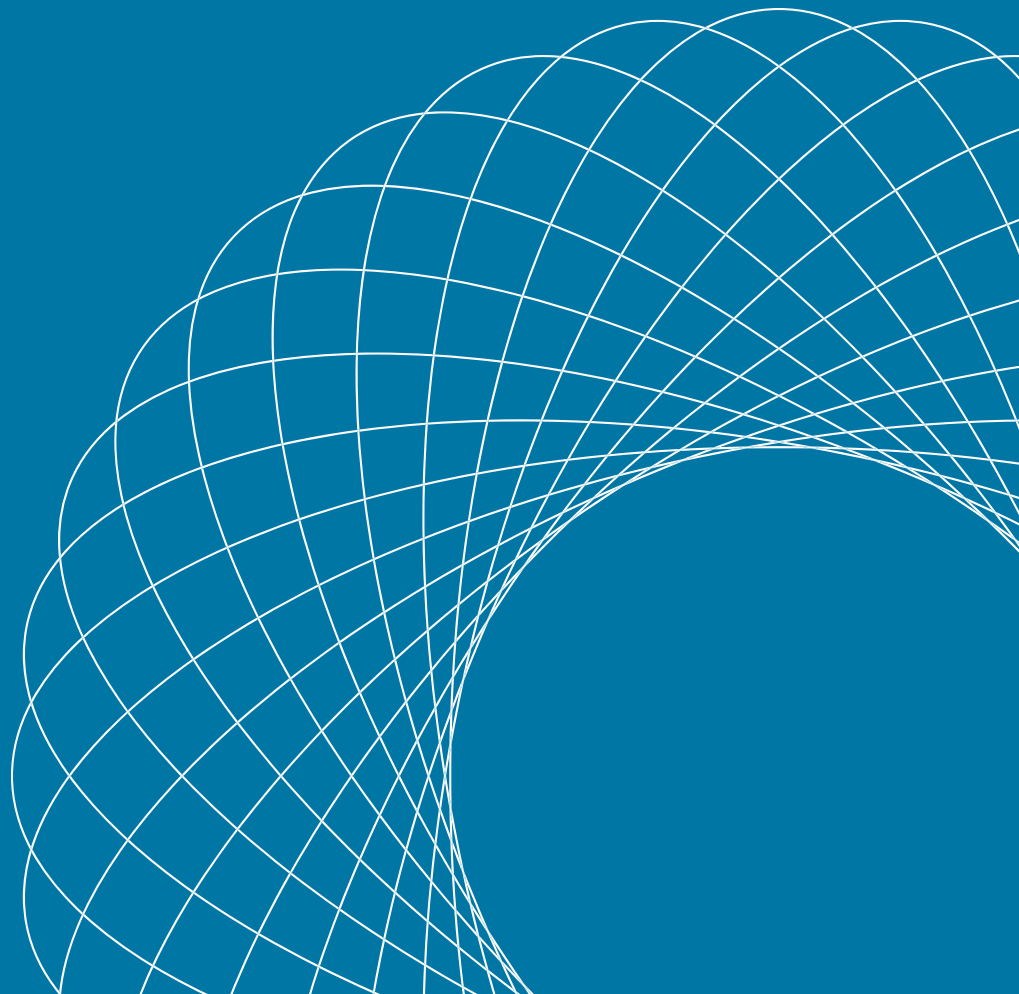


[1]Other responses:

- Consultant (2 mentions)
- IP
- Senior Lecturer

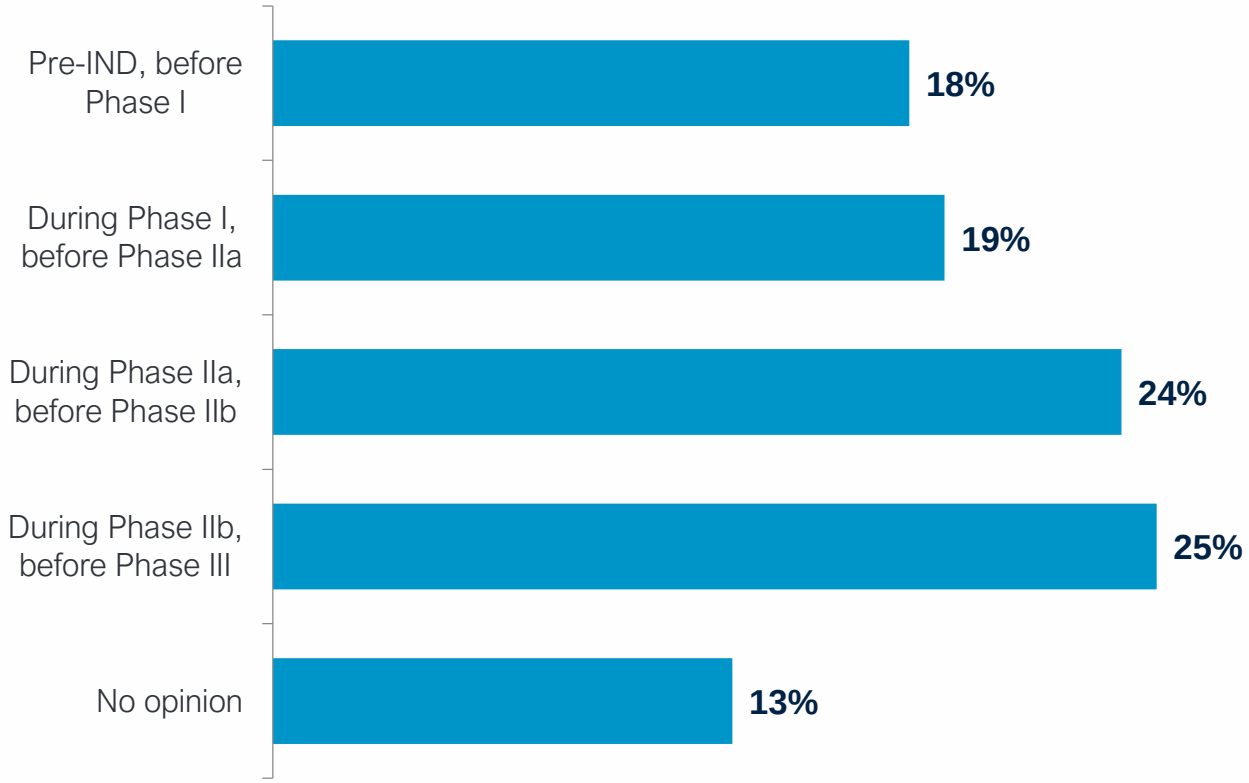
Base: All respondents (n=89).

Key Findings



Stage of Deployment of a 'Commercially Viable' Formulation

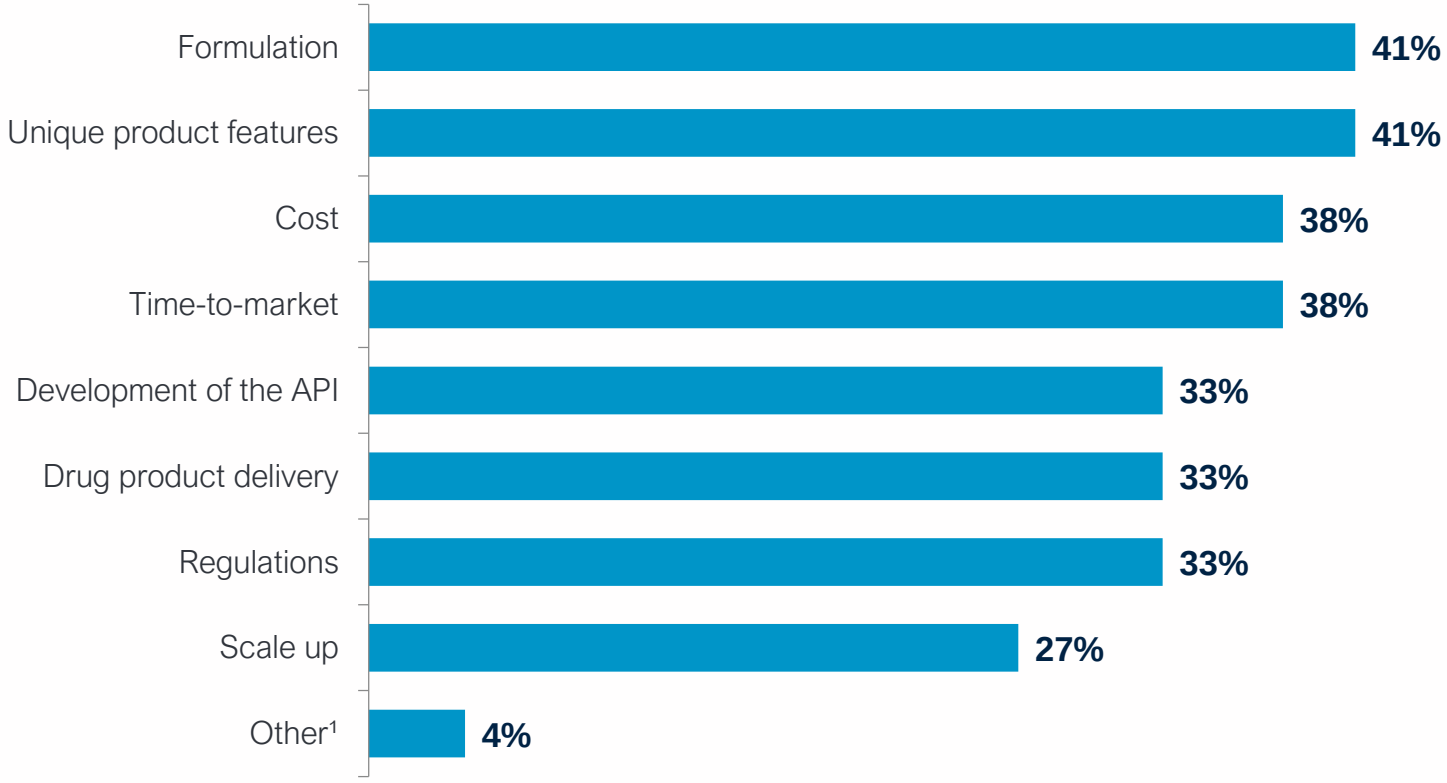
In which stage of the drug product development should a 'commercially viable' formulation be deployed?



Base: All respondents (n=150).

Top 3 Most Important Considerations in Drug Product Development

Please select the top 3 most important considerations in drug product development.



Base: All respondents; top three answers permitted (n=125).

[1]Other inc. Conduct clinical trials phase II, III and IV, Distributions, Ip, Limited distribution strategy & Providing an unmet need.

Choosing Certain Drug Product Development Considerations

Please explain why you have chosen those considerations?

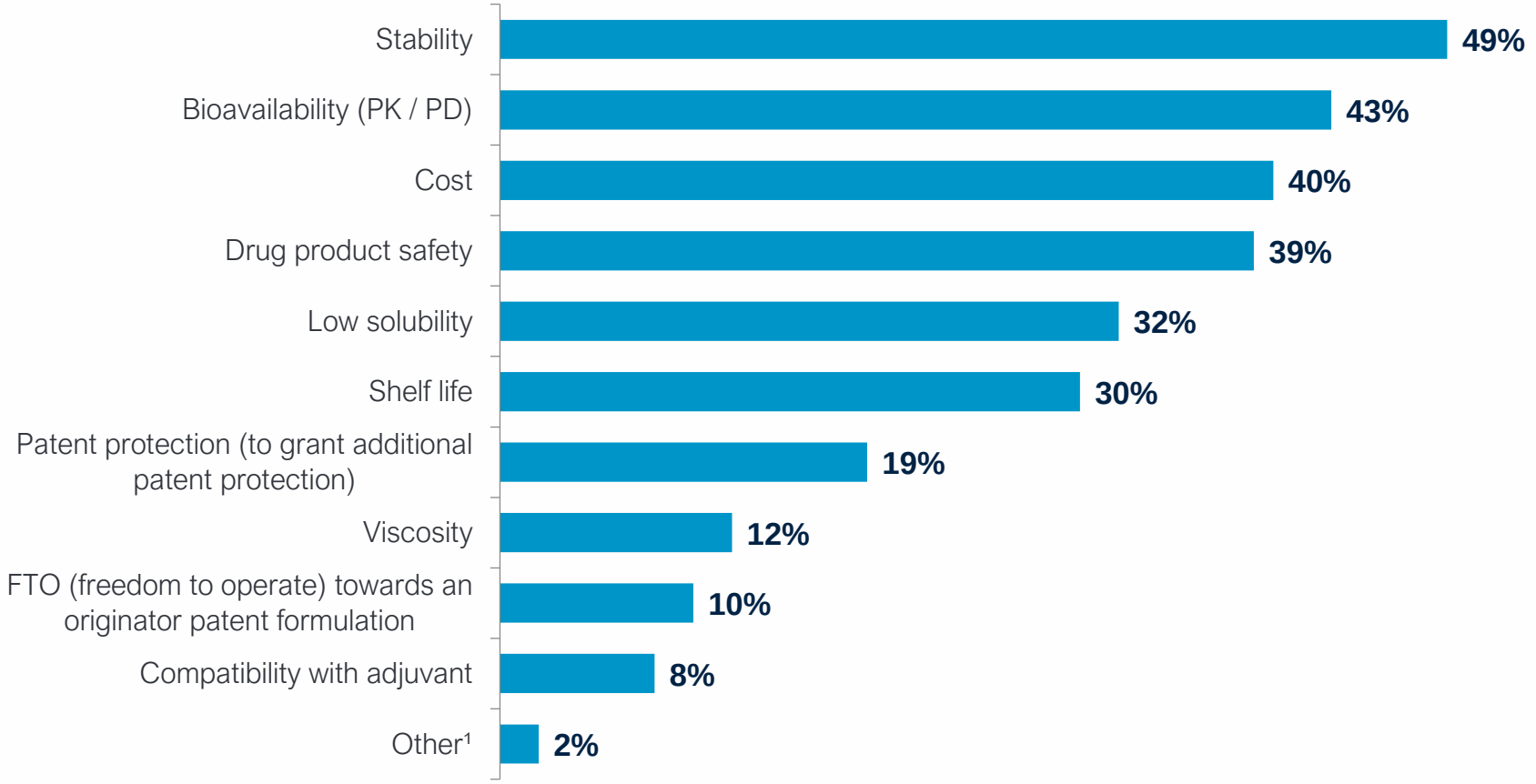
Reason for choice of the drug development considerations (*main themes from verbatim comments*)

1. Commercial viability: production and distribution of new drug to the market place
2. Market adoption: perceived 'best in class', uniqueness and simplicity of use
3. Regulatory compliance: approval process safeguards
4. Patient Realisation: meets a need, effectively targets cause and desired outcome

Base: All respondents (n=61).
Note: All verbatims can be found on slides 27-30.

Top 3 Formulation Challenges Faced

What are the top 3 formulation challenges you face?

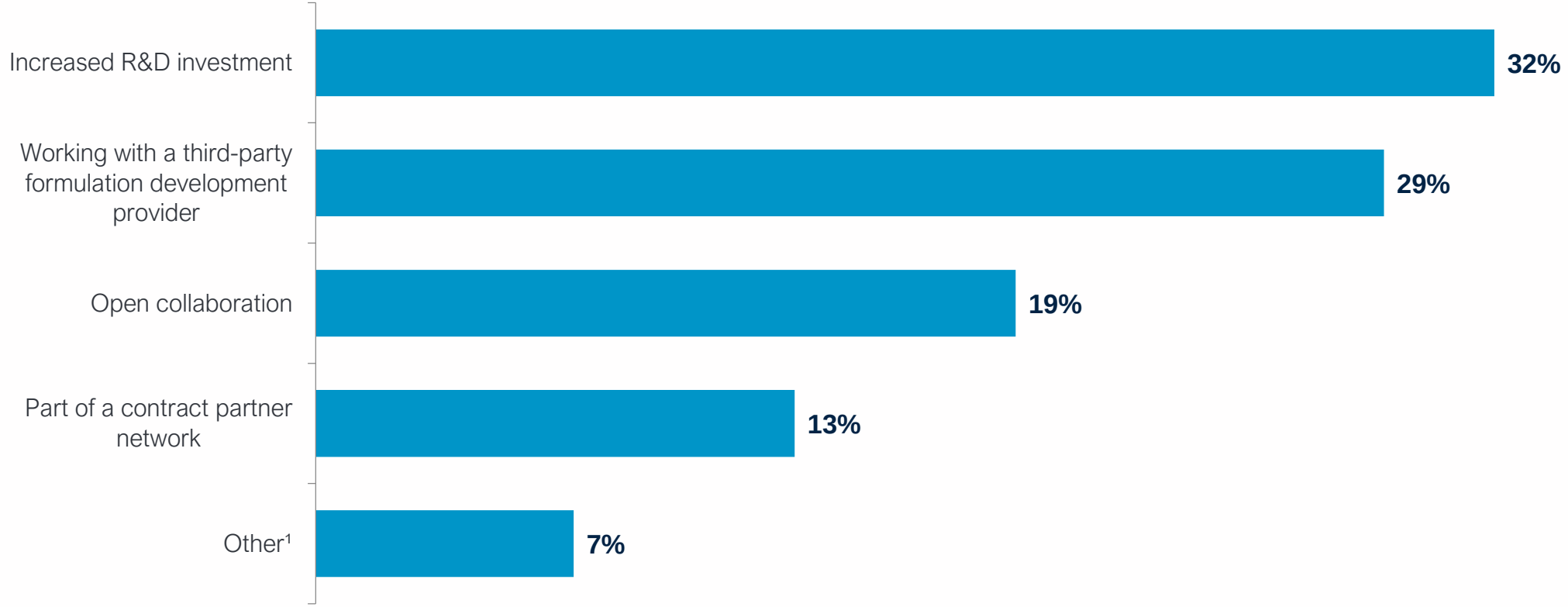


Base: All respondents; top three answers permitted (n=114).

[1]Other inc. Dosage & Not Applicable since we are a research site and conduct clinical trials phase I, II, III and IV.

Seeking to Overcome Formulation Challenges

How are you seeking to overcome your formulation challenges?

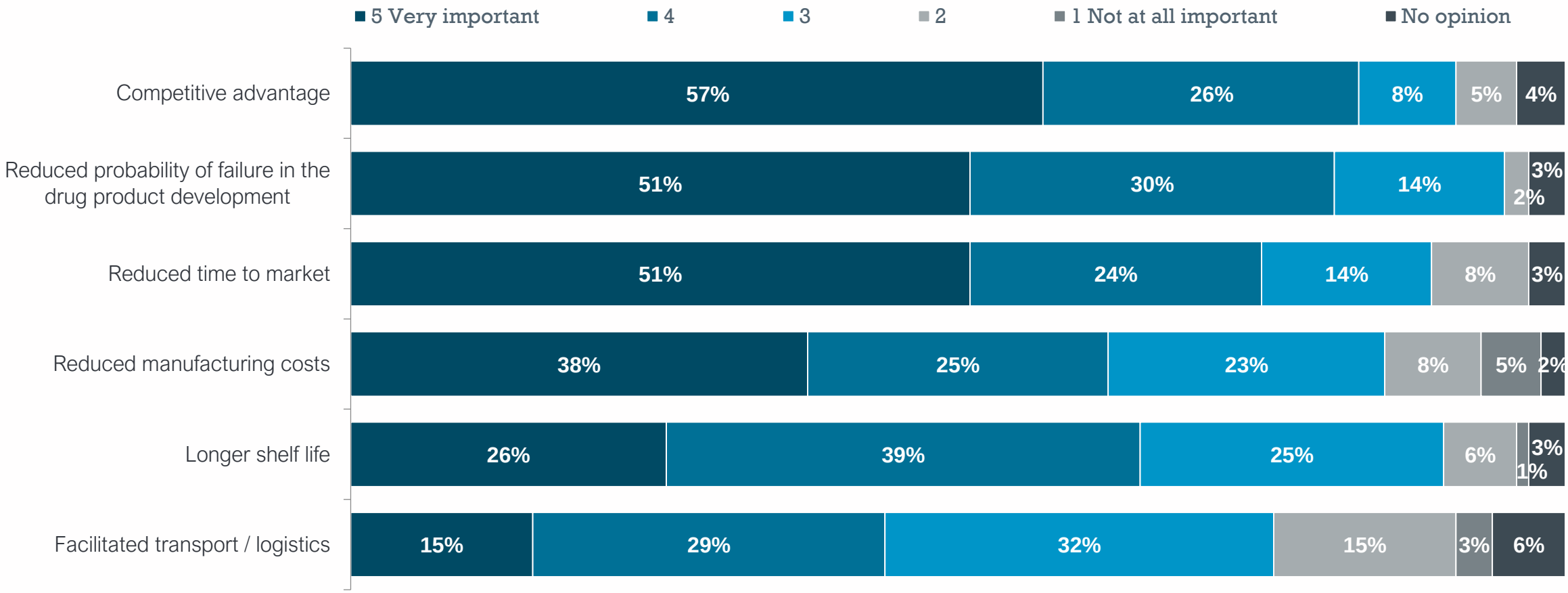


Base: All respondents; top three answers permitted (n=112).

[1]Other inc. All of the above, Contracting, Hiring best skilled people, My role is end user, so it's buying the product that meets those requirements, Not Applicable since we are a research site and conduct clinical trials phase I, II, III and IV & Process development improvements.

Importance of Aspects of Formulation

On a scale from 1 to 5, please rate the importance of the following aspects of formulation:

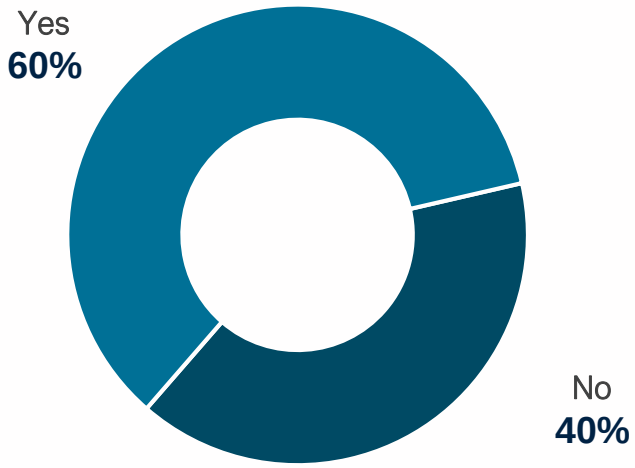


Base: All respondents (n=106).

[1]Note: top-two box : 5 Very important & 4 scores.

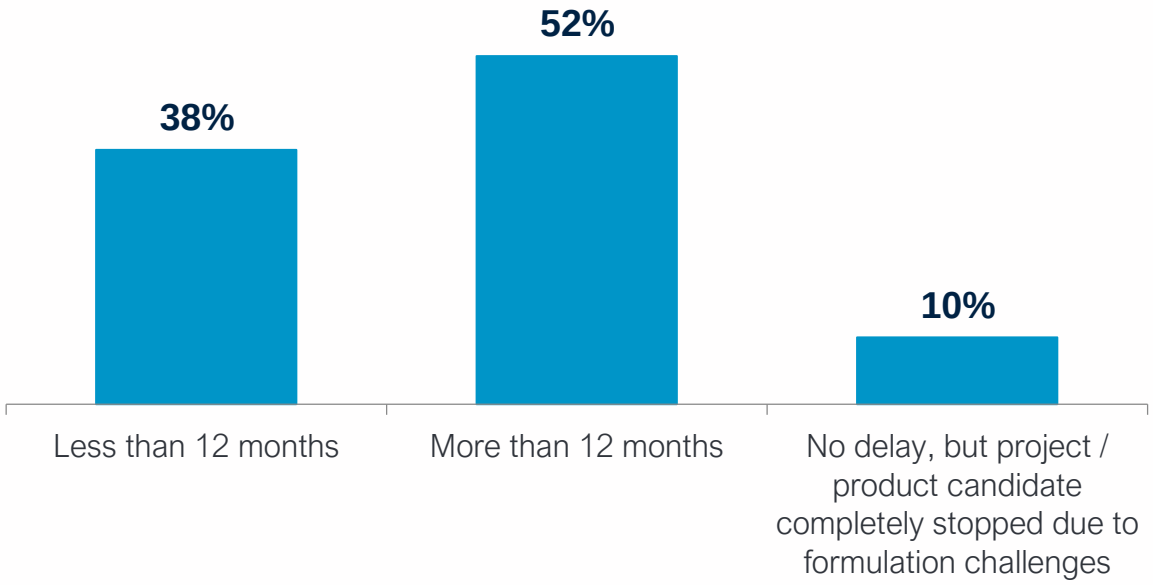
Project Failure or Delay Because of Formulation Challenges

Have you ever experienced a project failure or a significant delay, because of formulation challenges?



Base: All respondents (n=105).

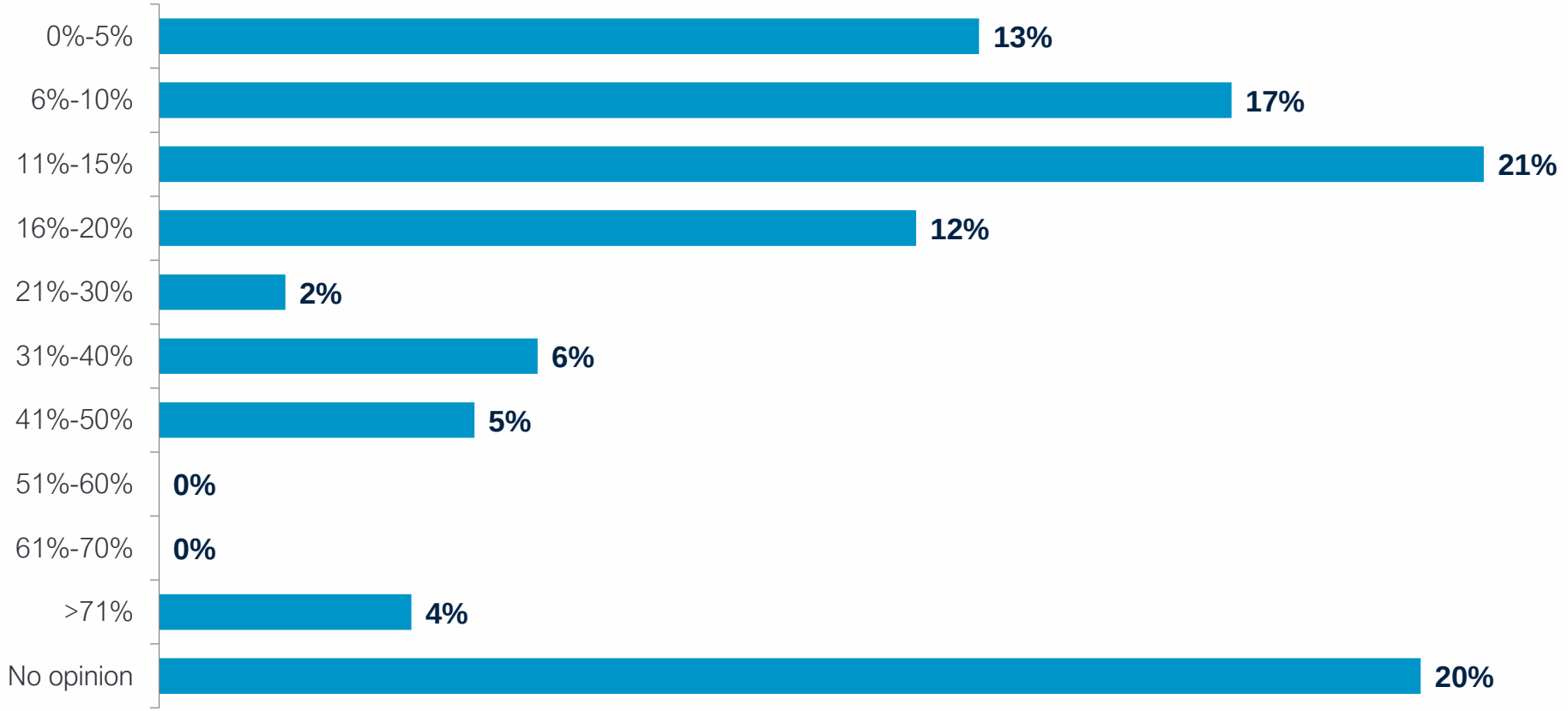
How long was the project delayed because of the formulation challenges?



Base: Respondents who experienced a project failure or delay (n=63).

Research and Development Budget Attributed to Formulation Development

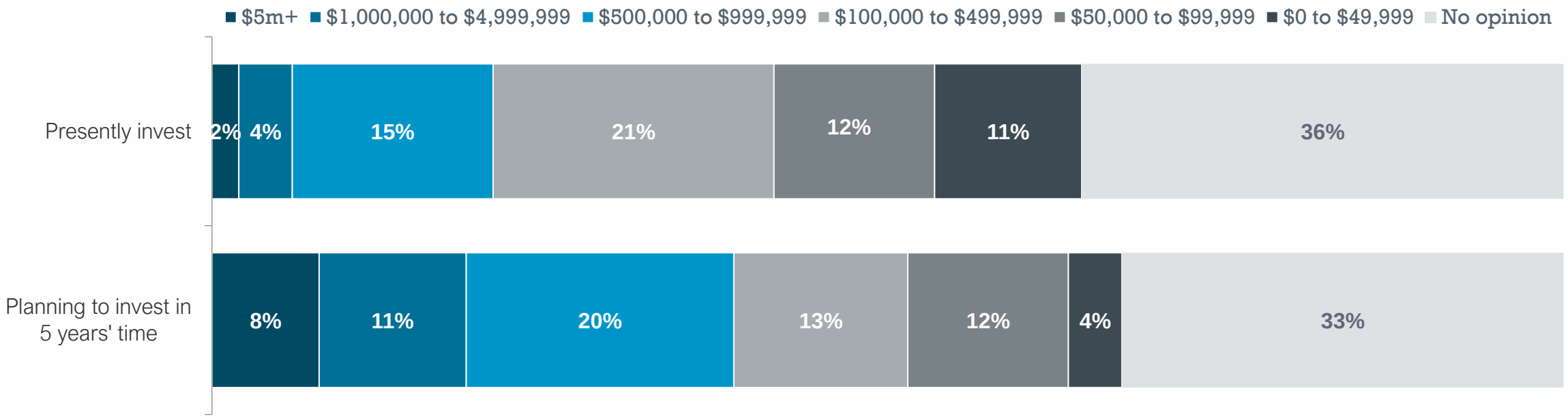
Approximately what proportion of your research and development budget is attributed to formulation development?



Base: All respondents (n=82).

Amount Invested Annually In Early Stage Formulation Per Project

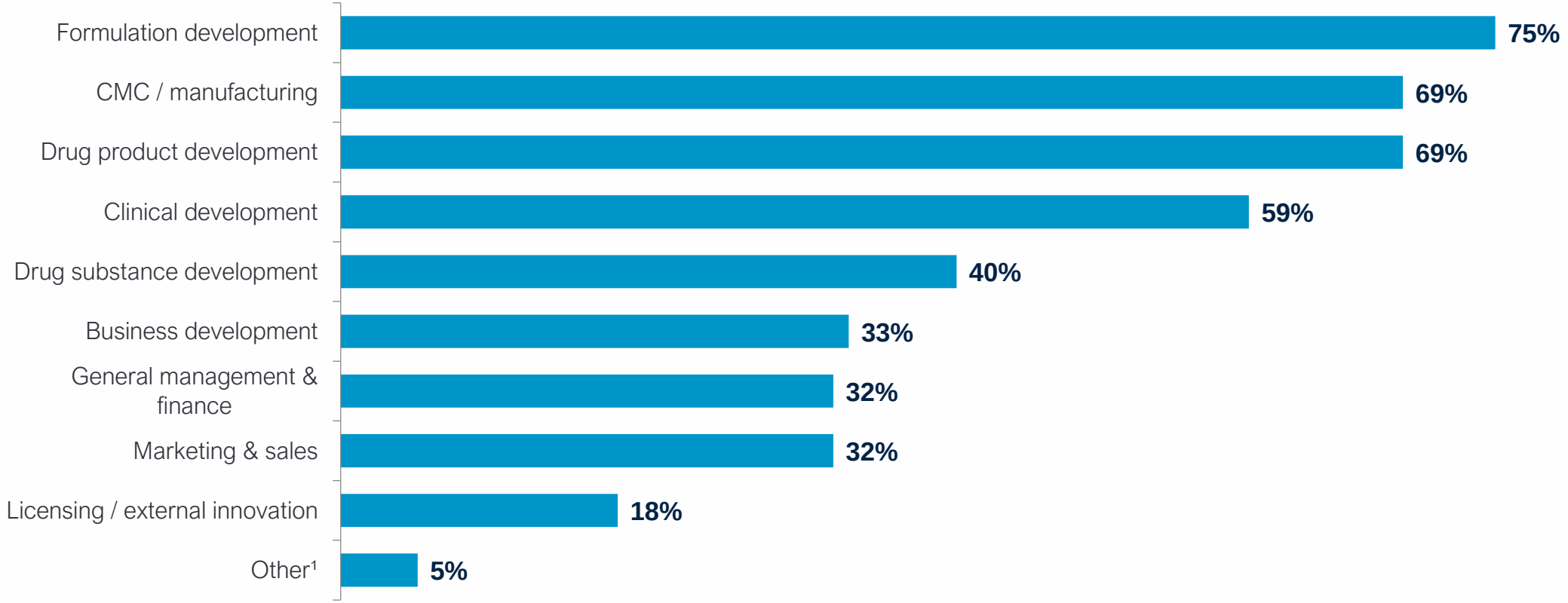
Approximately how much does your organization invest in early stage formulation per project annually? (US$)



Base: All respondents (n=95).

Departments Included in the Formulation Decision Making Process

Which departments are included in the formulation decision making process?

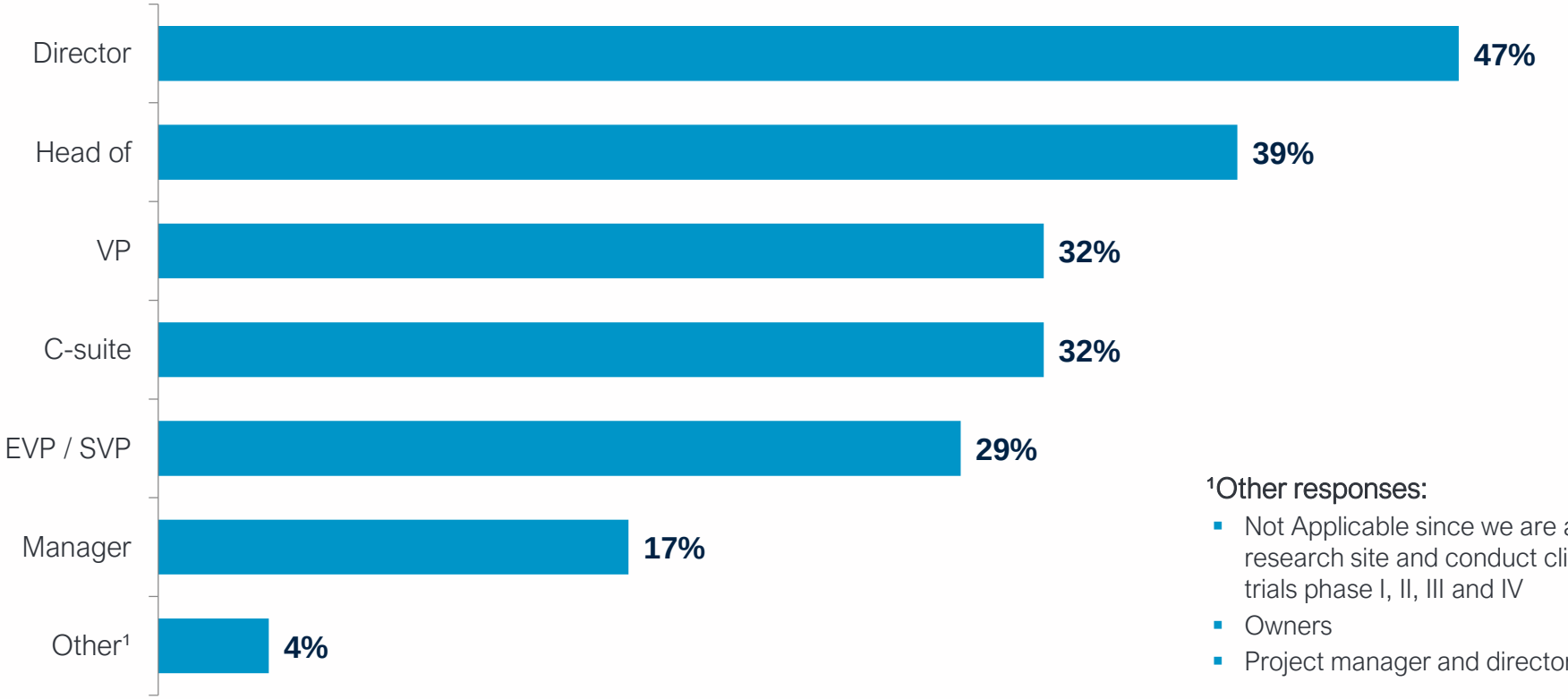


Base: All respondents; multiple answers permitted (n=93).

[1]Other inc. Not Applicable since we are a research site and conduct clinical trials phase I, II, III and IV, Quality Assurance, Regulatory & Regulatory affairs.

Key Decision Makers of the Formulation Process

Who are the key decision makers when it comes to the formulation process?



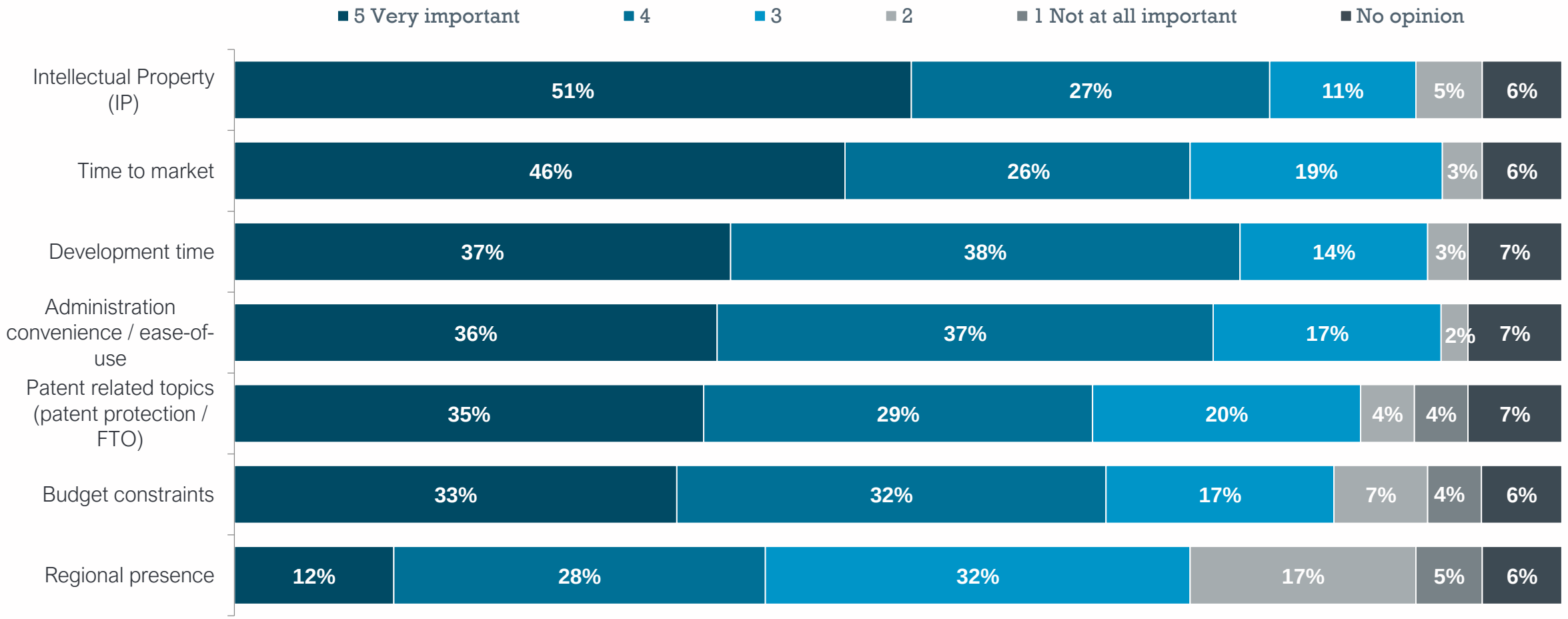
[1]Other responses:

- Not Applicable since we are a research site and conduct clinical trials phase I, II, III and IV
- Owners
- Project manager and director

Base: All respondents (n=96).

Important Considerations When Evaluating Formulation Strategy

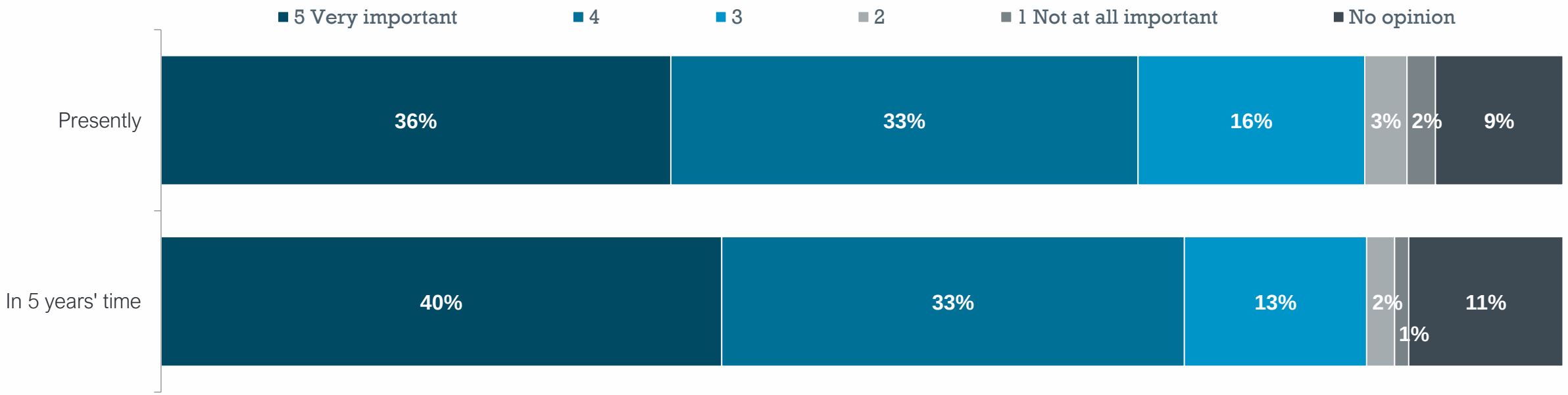
How important are the following considerations when evaluating your formulation strategy:



Base: All respondents (n=94).

Importance in Formulation / Reformulation to Commercial Success

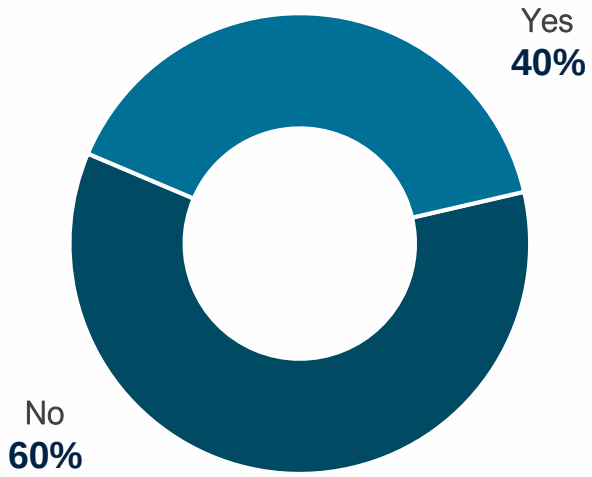
How important is formulation / reformulation to your organization's commercial success?



Base: All respondents (n=92).

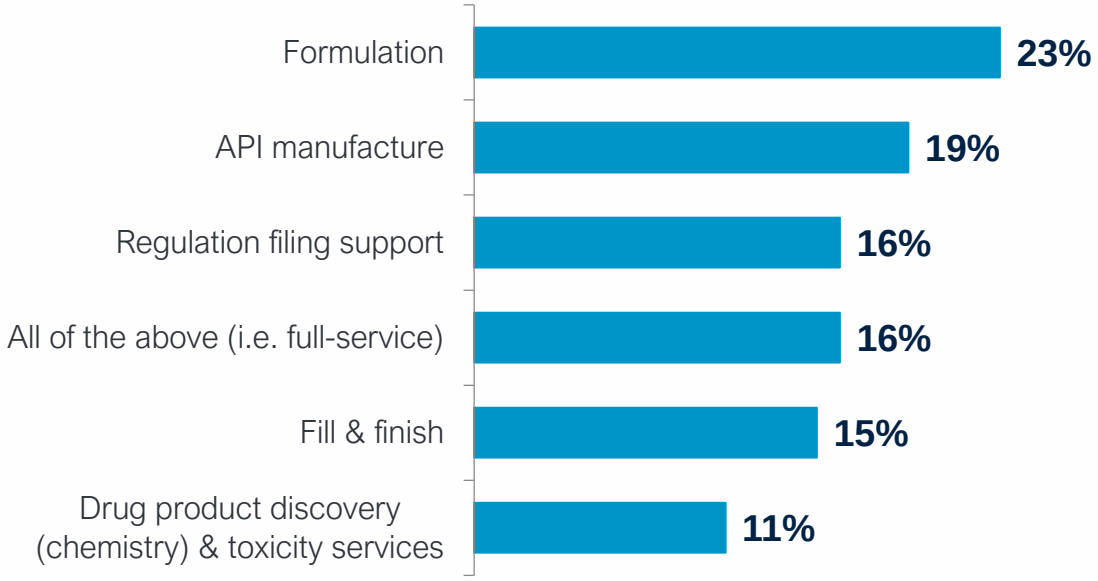
Outsourcing and Third-Party Manufacturer

Do you currently outsource your formulation development?



Base: All respondents (n=97).

What do you look for in a third-party manufacturer?



Base: All respondents (n=80).

Verbatim Comments

Choosing Certain Drug Product Development Considerations

Please explain why you have chosen those considerations (inc. considerations chosen[1]).

- Active ingredient is the most important factor in a drug product development, and formulation is a key factor followed by delivery of the drug product so it can effectively target the receptor/proper channel in the body for the drug to work. (*Development of the API / Formulation Drug product delivery*)
- "addressing a significant unserved patient need is the key. Nr 2 is to be able to deliver the product in a convenient way, again to serve the patient at best. Nr 3 is time-to-market". (*Time-to-market / Drug product delivery / Unique product features*)
- Affordability. (*Cost / Drug product delivery / Other (please specify): Distributions*)
- API is my input variability, formulation relate safety and efficacy while scaleup help knows my process issues. (*Development of the API / Scale up / Formulation*)
- API needs to be high quality in order to test clinical efficacy. Drug product development must adhere to regulatory minimum standards for manufacturing process and product quality. Development needs to consider how product will be stored, prepared by pharmacist, administered to patient, the fewer the barriers to simple and efficient use, drug formulary and prescribing decision making (i.e. therapeutic selection) will be based more on clinical and safety. (*Development of the API / Regulations / Drug product delivery*)
- API stipulates the efficacy and safety of the drug, so is formulation. It adds to bio-availability, and the easy usage of the drug is vital. (*Development of the API / Formulation / Drug product delivery*)
- COGS takes important part in the total cost. Pharmaceutical company should supply the sufficient amount of the drugs. (*Scale up / Cost / Regulations*)
- Commercial viability. (*Cost / Time-to-market / Unique product features*)
- "Cost consideration is prime for marketable product. Need to sell a quality product for a reasonable cost. Comply with all regulations, and it varies geographically. Unique features, I mean excellent medicinal properties with good therapeutic index". (*Cost / Regulations / Unique product features*)
- Development of the API is the first important point during the development of a product. The characterisation and targets of API have to be well defined. Then, formulation is important because the drug need to be stable and safe. Cost and market research have to be defined at the beginning of the product to be coherent. (*Development of the API / Formulation / Cost*)
- Determined by my background, and challenges I encountered in my career. (*Scale up / Formulation / Regulations*)
- Direct implant on commercialization. (*Scale up / Time-to-market / Drug product delivery*)
- Drug development has become competitive with focus on unique targets, delivery and high degree of safety, tolerability and efficacy. Reimbursement is very important too. (*Time-to-market / Regulations / Unique product* features)
- Due to Japanese pmda. (*Development of the API / Cost / Time-to-market*)
- First-in-class is the most important to get market-in. (*Time-to-market / Regulations / Unique product features*)
- "Formulation - safe non-toxic constituents most important scale up - the discovered/invented formulation should have similar efficacy levels while scaling up drug product delivery - there needs to be clear understanding of the effects of the drug dissemination & absorption by the body and drug development should be planned based on the drug's effect in the body". (*Scale up / Formulation / Drug product delivery*)
- Formulation is the most important part of the process. (*Formulation*)
- I feel that these three things, if not done properly (or unable to be done), will kill the program more than any of the other factors. (*Development of the API / Formulation / Drug product delivery*)
- I suggest that multiple products containing the same features is the past. One should look at the specific set of features. (*Development of the API / Cost / Unique product features*)
- I work in drug-device combinations and our biggest challenge is delivery. Also whether the 2 products will align appropriately for a timely launch. (*Formulation / Time-to-market / Drug product delivery*)
- If the product does not have qualities unique to the market, it better be priced more aggressively than its competitors. If the time to Market is excessive, it better a strong panel registration protection. With the delivery mechanism is poor on cumbersome then you can't get the product to Market. If this is the case all the rest other selections, I really Irrelevant. This is assuming that the product is legal and compliant or why even move forward with it? (*Time-to-market / Drug product delivery / Unique product features*)

[1] *Note: Original consideration question: Please select the top 3 most important considerations in drug product development.*

Choosing Certain Drug Product Development Considerations

Please explain why you have chosen those considerations (inc. considerations chosen[1]). (Continued…)

- If these change in late-stage development they have a large impact on time to file and/or time to market, which is a huge cost to the business. (*Scale up / Formulation / Regulations*)
- Many a good drug has died when hitting the commercial market because cost and product price wasn't practical in the disease state, drug product delivery is key to understand in the prescriber environment - if a drug requires special handling that is so far out the normal distribution and shipping channel that it is cost prohibitive for the drugs price point or not reasonable or practical for the prescriber or patient the drug will not gain market share. Unique product features need to be considered especially considering burden of taking the medication, too complicated, too many serious AE's the drug will not gain market share. (*Cost / Drug product delivery / Unique product features*)
- May fail, how administered and what it prevents. (*Time-to-market / Drug product delivery / Unique product features*)
- Most fit. (*Development of the API*)
- Must have a benefit over current products or else should not market. (*Formulation / Drug product delivery / Unique product features*)
- My goal is to create a "novel" drug to treat a "different" condition in a reasonable timeframe(less than 10 years). (*Formulation / Time-to-market / Unique product features*)
- "'Need to be first-in-class nearing in mind the competitor products.-need to consider price point when drug is marketed as costs are largely reimbursed." (*Scale up / Cost / Unique product features*)
- Patient access and soaring healthcare costs need to be addressed. Cost is a large factor when it comes to coverage or access for patients. Product delivery is also a driver of cost....nursing, training, infusion, REMS all drive up patient "convenience" factors which in turn decrease compliance to the therapy, and drive up overall cost for a patient or their insurance plan. There are too many "me too: biologics that offer no real efficacy or disease state treatment advantages. Also the biosimilar "craze" has been tempered by soaring product cost of development, so once those products reach market they really offer NO advantage to the brand product they seek to supplant in volume. (*Cost / Drug product delivery / Unique product features*)
- Regulation is the key of the product development, without the approval of the agency, we won't be able to launch the product. Time to market is also an importance factor since earlier to the market, doctors would be more familiar with it. Unique product features allows the sales and marketing team to pitch. (*Time-to-market / Regulations / Unique product features*)
- Scale up capability is clearly crucial to further development, choice of formulation may be important for future marketing considerations and ease of patient use. Regulations obviously need to be complied with. (*Scale up / Formulation / Regulations*)
- Stable, reliable drug product is one of the most important considerations to ensure patient supply. (*Development of the API / Scale up / Formulation*)
- Take for granted that the API is the basis for the development and then the formulation patent is ultra important and second to that is drug delivery when to decide the CDP. Scale up from clinical batches to commercial is another must to success. The time-to-market is decided by the CDP and COG is not an issue if it doesn't exceed 20%. (*Scale up / Formulation / Drug product delivery*)
- "The API is the first thing. The scale up is the great second place to invest. And finally the regulations is the real possibility for obtain a good result". (*Development of the API / Scale up / Regulations*)
- The formulation is the essence of a drug product that will determine how it delivers desired health outcome. Policy environments globally have placed more emphasis on cost. Time-to-market determines successful market entry, overcoming regulatory hurdles and reaching the target user. (*Formulation / Cost / Time-to-market*)
- The important points come and go according to the development stage. However, considering that we cannot change the API after we start clinical development, it is important to confirm whether the manufacturing process of the API can be established or not. In addition, considering that we cannot launch the product without complying the regulations, we cannot ignore the regulations during the clinical development as well as after the marketing. With regard to the cost, it might depend on the company's idea. (*Development of the API / Cost / Regulations*)

[1] *Note: Original consideration question: Please select the top 3 most important considerations in drug product development.*

Choosing Certain Drug Product Development Considerations

Please explain why you have chosen those considerations (inc. considerations chosen[1]). (Continued…)

- The most important considerations in developing a new drug product are that there is a need for a new product (providing an unmet need) and that it can be differentiated from existing products - without this it may not be registered and it is unlikely to be reimbursed by payers.
  Drug product delivery Unique product features Other (please specify): Providing an unmet need
- The other considerations do not lead to regulatory approval of the product and those considerations can be dealt with post-approval. (*Development of the API / Formulation / Regulations*)
- The product is dependent on the above characteristics and will need to take account of the unique features. While others such as regulations and cost are important, the above I consider the most important. (*Development of the API / Formulation / Unique product features*)
- These 3 items are the most necessary to determine success and commercial feasibility of a new product. (*Scale up / Regulations / Unique product features*)
- These are difficult questions, and I think the wisest approach is to consider each drug as an unique entity. (*Scale up / Formulation / Unique product features*)
- These are important aspects for any molecule to succeed. (*Formulation / Cost / Time-to-market*)
- These are most important in terms of stability. (*Development of the API / Formulation / Drug product delivery*)
- These are technical aspects that can be modified by company. (*Scale up / Formulation / Cost*)
- These are the most important. (*Scale up / Formulation / Drug product delivery*)
- These are the three barriers to drug development. (*Development of the API / Cost / Regulations*)
- These three are the most important differentiating factors in any product. (*Development of the API / Formulation / Drug product delivery*)
- This year has seen so many issues with shortages, a strong ability to scale up and deliver the drug will result in system confidence and adherence to scheduled vaccinations. Cost always has to be part of the consideration as many hospitals will end up paying up front for costs and then be reimbursed per their place in the market. (*Scale up / Cost / Drug product delivery*)
- "To be on regulation, in return to start. API characterizations the base. A ROBUST FORMULATION IS A THE WARRANTY." (*Development of the API / Formulation / Regulations*)
- Unique product features and time-to-market should be the priority to consider for any drug product development program, since these are the end of the program. We should begin with the end with any program. Regulations also must be considered. After we have these 3 established, all others will follow. (*Time-to-market / Regulations / Unique product features*)
- "Unless you have a USP you won't get accelerated approval or a good price. Particularly in gene and cell therapy biological really key Price is increasingly important and will become a real deal breaker for reimbursement ". (*Scale up / Cost / Unique product features*)
- We consider these points during pj management. (*Time-to-market / Regulations / Unique product features*)
- Without an API there is no project. Formulation can be a stumbling block -- it's best to know and solve my formulation issues early in the product development process. Uniqueness is required for product differentiation in the marketplace. (*Development of the API / Formulation / Unique product features*)
- Without an API, there is no drug product for development. Formulation is always a challenge. Thus, it is best to determine if formulation will be an issue. "Time is money. (*Development of the API / Formulation / Time-to-market*)
- "Without API there is no drug product. Formulation is essential to drug product delivery and an essential component of QbD. Proper DP delivery parameters reduces patient risk." (*Development of the API / Formulation / Drug product delivery*)
- Without consistent, efficient API production and stable formulation, there will be no drug product to take to market. (*Development of the API / Scale up / Formulation*)
- Without Unique featured, lower Price and less Volume Potential. API needs to be cost feasible. Regulations must be Met. (*Development of the API / Regulations /Unique product features*)
- "Without unique features there is no innovation to sell into the system, so it doesn't matter what the cost is if no one needs it. Product delivery can be differentiator or a noose around ones neck, that can be exploited to followers - make sure the formulation and posology works for the patient, or market share will be quickly lost". (*Formulation / Drug product delivery / Unique product features*

[1] *Note: Original consideration question: Please select the top 3 most important considerations in drug product development.*

Choosing Certain Drug Product Development Considerations

Please explain why you have chosen those considerations (inc. considerations chosen[1]). (Continued…)

- Work with highly potent molecules - cytotoxic - limits number of vendors can work with. (*Formulation / Cost / Unique product features*)
- "You have to satisfy the regulatory authorities. If you don't you won't be allowed to market the product. You have to be able to make enough of the product and at a viable cost. Otherwise you cannot will not have a commercially viable product.“ (*Scale up / Cost / Regulations*)
- You need to have new innovation drug which can be manufactured and you need to ip around you new product to be able to it financed. (Scale up / Unique product features / Other (please specify)

[1] *Note: Original consideration question: Please select the top 3 most important considerations in drug product development.*

Contacts:

Rentschler Biopharma SE
Dr. Frank Mathias
CEO
e-mail: communications@rentschler-biopharma.com

LEUKOCARE AG
Michael Scholl
CEO
e-mail: michael.scholl@leukocare.com

Media Inquiries:

MC Services AG
Eva Bauer
phone: +49-89-210228-0
e-mail: rentschler@mc-services.eu

The "2018 Survey Formulation in the Drug Development Process" was first published on November 6th, 2018