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MEDPACE

WINNING AT YOUR DRUG DEVELOPMENT STRATEGY

A Playbook For Emerging Biotechs

TABLE OF CONTENTS

WHAT YOU WILL LEARN IN THIS REPORT

- The global biotech industry continues to witness growth with an estimated market size of nearly $300B, despite the current state of the funding environment
- Globally, emerging biotechs are taking control of drug development pipelines
- To be competitive, biotechs should have a strong strategy in place
- Strategic planning can provide flexibility, mitigate risks, and increase chances of success
- Choosing the correct biomarkers is an integral part of laboratory strategy
- How to understand and react to the consequences of inadequate strategic planning in therapeutic development
- Engaging with the regulatory authorities from an early stage will help avoid obstacles later on during drug development
- Identifying the right strategic partner for your drug development process

THE ROLE OF EMERGING BIOTECHS IN THE INDUSTRY TODAY

In 2021, the global biotech industry surged to an estimated market size of $300B[1]. Following a year of vigorous growth and momentous funding, the biotech industry is now facing a shift in the funding environment, provoking challenges that require careful navigation. Despite the evolving landscape of funding, biotech remains the life science industry's pinnacle of innovation and growth. Over the last 10 years, the overall drug R&D pipeline has grown 85%, with contributions by emerging biotechs responsible for 89% of this growth. In 2021, 42% of drugs filed with the FDA were registered by emerging biotechs[2].

Throughout the modern biotechnology era, young and pioneering biotechs have led discovery while being reliant on big pharma to bring products to market. These collaborations are highly productive, as the most successful drugs launched between 2016 and 2020 were those originated by emerging biotechs but launched by larger companies; by their second year on the market, median sales were seven times higher than those of other drug launches[2].

Other partners are also entering the field. **Recent years have seen a shift away from big pharma developing drugs alone to companies working in collaboration with contract research organizations (CROs), contract manufacturing organizations (CMOs), and contract development and manufacturing organizations (CDMOs).** A 2022 survey conducted by BioPlan Associates revealed that 86.9% of biopharma respondents outsourced activities[3].

Despite these collaboration opportunities, emerging biotechs face a large part of drug development on their own. Before engaging with a suitable partner, biotechs have to decide on a strategy for their drug development project and clarify their end goals. And there is a lot at stake. **A carefully planned strategy can improve the chances of a drug's success, whereas mistakes can result in loss of money, prolonged timelines, and even failure of the development program.**

Therefore, a solid drug development strategy is of paramount importance. This playbook is designed as a sequel to "A Toolkit for Emerging Biotechs" created by Medpace and Labiotech, and will guide you through the most important steps of planning a successful drug development strategy.

$300B

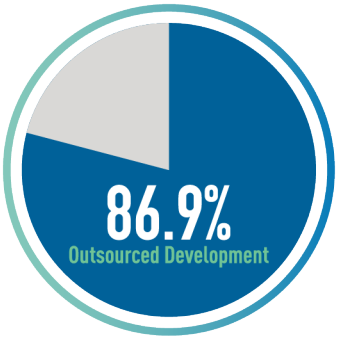
Global Biotech Estimated Market Size in 2021

42%

Drugs Filed with the FDA were Registered by Emerging Biotechs

Survey Response:

Drug Development Activity - Biopharma Industry



THE IMPORTANCE OF STRATEGIC PLANNING

"The ultimate goal of strategic planning is to embed flexibility in your drug development program."

- Reinilde Heyrman, MD, *Chief Medical Officer, Medical Department*

When biotechs first start out on their drug development journey, a strategy can be seen as a safety net. Strategic planning early on can force a company to recognize its goals and communicate these goals within the organization as well as with the outside world. Why is this so important?

As emerging biotechs rely heavily on funding, being able to efficiently communicate the goals of a drug development project to potential and dedicated investors can secure financing and provide reassurance. "Doing strategic planning early on in development is really important because it allows you to tell your story to people who hopefully will invest in your organization," confirms Reinilde Heyrman, Chief Medical Officer of the Medical Department at Medpace.

Also, **defining goals in early strategic planning can help a company delegate decision-making processes.** At this stage, a company can decide how it wants to accomplish its goals and what its values are, which will allow people to act fast if unexpected changes occur throughout the drug development project — a likely scenario.

"No strategic planning is ever useful if there is no execution of the plan," Heyrman adds. "Not just doing strategic planning early on, knowing what needs to be executed, and in what time frame, but also how we will accomplish all of these steps. Never forget: if you fail to plan, you plan to fail."

WHY IS STRATEGIC PLANNING IMPORTANT?

- Recognizing the goals of the drug development project
- Communicating goals within the company and outside
- Securing funding and investor relationships
- Delegating decision-making processes
- Understanding how goals can be accomplished and executed
- Reducing risks throughout drug development

Heyrman emphasizes the importance of strategic planning if one considers the consequences of inaccurate strategic planning or no planning at all. With no goal to work towards, the motivation of staff could suffer. This, in turn, could lead to problems with retaining good experts for the company. Moreover, **inaccurate strategic planning could result in inefficient investments and a lack of resources.** This goes hand-in-hand with an uneven distribution of tasks and processes, limiting innovation and creativity.

"Without a shared vision or goal, management will have difficulties maintaining control over the organization," says Heyrman. "Everybody may go off in a different direction because that seems to be the right way for that person. If we don't have a plan about what we want to accomplish, how will we accomplish anything?"

To ensure that strategic planning goes well, biotechs need to follow a number of different steps. One of the most important factors to keep in mind when planning a strategy is honesty, says Heyrman.

"You have to be absolutely truthful with yourself. What are the drawbacks of your compound? If you can foresee these, you can address them in your development plan. If, for example, you know that there may be an effect on liver enzymes, make sure to address it early. It's better to have it figured out during development, rather than having a major disaster on your hands after coming to market."

Also, biotechs should always try to think outside the box. It can help to observe the medical environment, ask what investors want, and what patients and physicians need. Additionally, clearly identifying what competencies are available in-house and what expertise is lacking will be critical to the organization's success. Hence, knowing and allocating the necessary resources, even for future steps of the project, should be part of the strategy.

At the heart of it all lies communication. Through communication, managers can make sure that everybody in the company, as well as other stakeholders, knows what the goal is and how it will be achieved.

Understanding goals and mapping them effectively to timelines is essential in strategic planning. What is the sequence of events? What are the dependencies? What is exploratory/nice to have vs. what is absolutely necessary to move to the next step? "Being thoughtful with planning to ensure you are getting what is needed without additional noise is key. Introducing nice to haves can impact timelines. On the other hand, if you are trying to expedite timelines you have to be careful you are not omitting key items that will be challenging to incorporate later down the line," says Jennifer Gehlhar, Senior Vice President of Clinical Trial Management at Medpace.

KEY POINTS TO CONSIDER DURING STRATEGIC PLANNING

- Be honest at all stages
- Observe what patients and physicians need
- Try to balance risk during planning
- Consider timelines and stacking of events
- Know and allocate your resources well
- Communicate openly with your staff and stakeholders

Closely related to time management—and something that is common for drugs with an orphan drug designation—is the so-called stacking of events. Here, timelines are compressed, which shifts processes and responsibilities. "Ensuring appropriate resource allocation to manage shortened timelines for the same amount of work will allow you to stay on target and remain nimble," says Gehlhar.

The development plan also has to prepare a company for unexpected changes. "While the long term strategy should be relatively static, the development plan is not a one-time exercise that we can leave in the drawer until we're done with the project," says Heyrman. "It is a living document. Whenever the environment or situation changes, think about the kind of repercussions this will have on your strategy and how you can adequately react to what is happening. Continuously evaluate the environment to identify new opportunities either for the company or for the compound."

WHAT TO CONSIDER WHEN PLANNING A STRATEGY

Besides time management, resource allocation, and communication, strategic planning also involves a number of different compound development stages. These include the establishment of a medical or laboratory strategy; a therapeutic development strategy; and understanding and planning for regulatory processes.

LABORATORY MANAGEMENT

"The benefit of identifying and utilizing the correct biomarkers is the facilitation of the development of safer and more effective drugs."

- Jerry Becker, MBA, *Director of Laboratory Scientific Affairs*

Critical to laboratory strategy are the correct biomarkers. **A biomarker can support efficacy studies, eliminate unnecessary testing, help identify and understand patient populations, support the choice of different cell lines, and make drugs safer.** In short, "a well-established biomarker can save you a lot of headaches," says Jerry Becker, Director of Laboratory Scientific Affairs at Medpace.

"Choosing the correct biomarkers for a study is important to make sure the new therapeutic has the desired efficacy results," adds Becker. "This helps the study and program to stay on target with timelines without the additional time needed to add extra biomarkers. Getting it right early saves costs by eliminating unnecessary testing."

The key challenge lies in determining the most suitable biomarkers. And according to Becker, a strong laboratory partner can help. This partner can not only support a biotech in finding the best biomarkers, but also help it choose the right analytical method as well as the best regulatory approach, for example, to decide between following Good Clinical Laboratory Practice (GCLP) or Good Laboratory Practice (GLP)[4].

THE ROLE OF BIOMARKERS IN LABORATORY MANAGEMENT

- Supporting safety and efficacy studies
- Eliminating unnecessary testing, thereby shortening timelines and saving costs
- Identifying and understanding patient populations
- Helping to choose viable cell lines

Moreover, **a laboratory partner can support the biotech in developing solid plans for study execution.** "Biotechs working with a central laboratory have the added benefit of having studies managed by seasoned project managers, who know how to design a study that allows the collection of quality samples, build kits with the required materials, and provide instructions to the clinical sites for collection, processing, and shipping needed for biomarker testing," Becker explains.

To make sure that the selected biomarkers work, biotechs also have to choose the correct analytical method. Factors such as sensitivity and measuring ranges need to be taken into account. In order to select the right analytical method, it is necessary to understand a study's patient population as well as how the study indication affects the levels of the analyte, says Becker.

"The most useful biomarkers should be suitably qualified and easy to collect with adequate stability to ensure that they can be processed, transported, and analyzed while delivering accurate and reliable data," Becker concludes.

THERAPEUTIC DEVELOPMENT

Therapeutic development includes multiple activities put in place to support the clinical development plan including non-clinical in vitro and in vivo studies, manufacturing, and clinical pharmacology assessments.

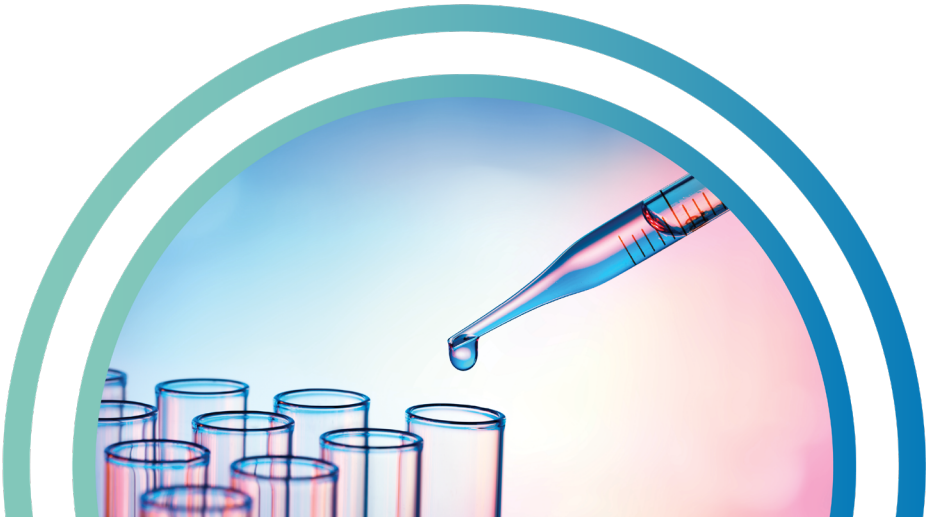
Keeping up rigorous strategic planning throughout therapeutic development is important for many reasons. "It's critical that you have the right strategy in place when you start your manufacturing or your non-clinical development program," says Heyrman. "The keyword here is flexibility. Even while you're still in the strategic planning phase, you want to make sure you're designing your manufacturing and non-clinical programs to ensure that you can do what you planned when you get to the clinical phase."

Establishing development targets early and developing an appreciation for the clinical program will allow efficiency within the program. Understanding the future needs of a program from a clinical perspective can help a biotech design what needs to be done early on.

Heyrman adds: "The last thing you want to do is to get to the clinic and be limited to what you can do because of the limitations of the non-clinical study duration or stability data. Let your clinical plan drive your non-clinical and manufacturing program, not the other way around."

To achieve this, biotechs should follow phase-appropriate development. **For each phase, a company should understand the information needed to support the current phase of development, as well as its impact on future opportunities. At the same time, resources have to be balanced, which is something small biotech and pharma companies have to do more than big pharma, due to fewer resources.**

"Understanding the key program risks based upon the knowledge of your product and the indication, and balancing resources to proactively address critical risks and gaps at the appropriate time is key," says Heyrman.



CONSEQUENCES OF INADEQUATE STRATEGIC PLANNING IN THERAPEUTIC DEVELOPMENT

Problem: Biotechs often focus on single approaches, don't mitigate risks, and don't have contingency plans in place.

The scenario:
An emerging biotech has collected enough information and resources to get its product to the clinic. But then it discovers that it hasn't considered upscaling. So it suddenly has a product that cannot be produced in big batch sizes.

"Large companies may have a lot of different systems in place—running additional cell lines, running other optimization columns—so that they have potential solutions should a primary fail. They develop backup systems and scenarios. Oftentimes, we don't see that with smaller companies because it's expensive. If it fails, it fails, and they end up with significant delays to their program," says Heyrman.

Consequences:
- Significant delays
- High costs
- Failure at different stages of the development program

What can be done to prevent this outcome?
- Look for different approaches, not just a single approach
- Understand the critical aspects of your program and allocate resources accordingly
- Answer the right questions at the right time to give yourself more flexibility
- Be agile and enable the repositioning of your program if an obstacle comes up

Of special interest to biotechs working in the rare and orphan development space, two issues that can contribute to market non-approvals are related to the risk-benefit profile and/or manufacturing concerns for the compound.

First, smaller or limited clinical indications may result in inadequate characterizations of the patient population which could negatively affect product labeling. Second, due to fewer opportunities to manufacture batches of the compound over time, there may be an inadequate understanding of the drug's manufacturing process. Control and consistency are important to the regulatory authorities, but they can be a challenge.

REGULATORY PROCESSES & EARLY SCIENTIFIC ADVICE CONSIDERATIONS

"It is critical from a manufacturing, preclinical, and clinical perspective that biotechs outline their plan to regulators to receive feedback, so as they move forward, there is general alignment."

- **Brad Hansman,** *Vice President, Site Activation & Maintenance*

Regulatory processes for global clinical trials can be complex, and therefore require careful consideration and strategic planning. Initiation of regulatory interactions frequently occurs via a request for scientific advice. Scientific advice permits the company to receive critical feedback from regulators throughout development.

The timing and appropriateness of requesting scientific advice should be considered for each region based on the strategic plan and objectives of the proposed meeting. Typically, scientific advice is particularly important when reaching key milestones, such as before submitting an investigative new drug (IND) in the US, at the end of phase II, and prior to submitting a marketing application.

In fact, **early alignment with the regulatory authorities sets the stage for achieving alignment, and is often essential to prevent unexpected or additional development activities or a delay in initiating clinical trials or receiving marketing approval.** By providing a detailed plan and communicating early with the regulatory authorities, drug developers can receive feedback that enables the progress of clinical trials and ensures the biotech has understood the regulator's perspective on the proposed development plan.

"From a US perspective, biotechs should typically engage with the FDA once their initial preclinical work is completed and they're ready to go into the first in-human studies," explains Brad Hansman, Vice President of Site Activation & Maintenance at Medpace. "They should request a pre-IND meeting with the FDA to present the current CMC (chemical, manufacturing, and control) and preclinical data or plans, in combination with the phase I clinical trial design."

This allows the biotech to receive feedback on the collected data as well as the trial design early on, before initiating in-human studies. Moreover, when it comes to developing innovative investigational products such as biologics, biotechs have the possibility to engage with the FDA in so-called INTERACT meetings even earlier during preclinical stages[5]. In INTERACT meetings, biotechs can receive advice on CMC, toxicology, and pharmacology, as well as clinical sections of the development program from FDA officials.

In Europe, the EMA also supports early engagement. "The EMA actually endorses early engagement with them," says Hansman. "That includes giving scientific advice and protocol assistance. But they are not just simply looking at the product as a whole, but also at the quality, and non-clinical and clinical plans."

Although the EMA is the governing authority in Europe with its own processes and procedures, each European country also comes with its own national authority. Examples include the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK and the Federal Institute for Drugs and Medical Devices (BfArM) in Germany[6][7].

Of course, there are also biotechs that want to work and/or market both in the US and Europe. "For this situation, there is a scheme where biotechs can receive dual scientific advice from both authorities at the same time," Hansman explains. "This will allow you to harmonize the information and scientific advice received at early stages and adjust your plans accordingly."

While engaging with the regulatory authorities early on is important for every drug developer, it is paramount for those working on a rare or orphan disease indication or on a therapeutic indication with a high unmet medical need. In this case, early engagement can provide information information on which stages the authorities might be willing to be more flexible, says Hansman.

“You’re getting feedback early on in the process to enable more streamlined clinical development that may lead to an agreement. So instead of running multiple phase II and phase III trials, you could get away with a single pivotal trial to support marketing approval for a particular indication, for example,” says Hansman.

Sometimes, biotechs are working with such state-of-the-art technologies that there are no defined regulatory processes in place yet. It is thus essential to work closely with the regulatory agencies. A biotech should try to understand the competitive landscape. Namely, whether it is actually the first in that particular space or whether there are other competitors in the space but none of them have approved or marketed the technology yet.

“It’s important to understand this upfront because sometimes you can gain competitive intelligence from what’s publicly available and that’s really important,” Hansman explains. “If there’s a scenario where you’re truly the first and you’re sort of creating as you go along, then that’s when it’s critical to look for additional regulatory interactions. Where there is no pathway established, the agency will be more willing to engage and to help define the pathway, particularly from a clinical safety and efficacy perspective.”

“If you’re working on cutting edge technology, productive discussions with regulators are critical early on,” adds Heyrman. “You’re the expert of this novel technology so you are responsible for getting the agency on board early to show that you have the appropriate level of characterization and understanding of risk of your product.”

When facing these situations, a biotech company can greatly benefit from having a partner at its side. An experienced partner will know what the regulatory authorities need and can make the biotech aware of the necessary requirements and steps.

MANAGING STRATEGIC PARTNERS

"The ultimate goal of strategic planning is to embed flexibility in your drug development program."

- Reinilde Heyrman, MD, *Chief Medical Officer, Medical Department*

Bringing in a strategic partner can help a biotech immensely throughout its drug development project. But when is the best time to get a partner involved? When is too early? When is too late?

"You should start looking for a strategic partner once you've identified your lead compound. It's important to have a strategic partner in place early on because they can help you identify landmines and understand challenges that could become an issue from a manufacturing perspective or from a non-clinical perspective, and understanding how that aligns with your clinical development plan and regulatory expectations," says Hansman.

Although partners can be a valuable support for biotechs, sometimes there is different or conflicting advice coming from different partners. This can be extremely confusing, especially for a biotech with little or no drug development experience.

"There may occur what I call the 'analysis paralysis,'" says Heyrman. "The biotech has to understand that in the end, it will have to make the ultimate decision. Always keep in mind that every advisor has their own agenda—it may be conscious, it may be subconscious—but as the Sponsor, you make the ultimate decision. When you get all that advice, it's good to evaluate it against each other. It's kind of like being a detective in search of the truth."

At the same time, Heyrman emphasizes that the biotech has to keep an open mind. First, it may hear things it doesn't want to hear. More importantly, it may have to read between the lines and understand those things that haven't been said.

"In these situations, I always think of the story of the Emperor's New Clothes," Heyrman explains. "If you only hear everything that fits within your preconceived notion, without paying attention to what you would prefer not to hear, you may be in a situation that, like the emperor, you end up without any clothes."

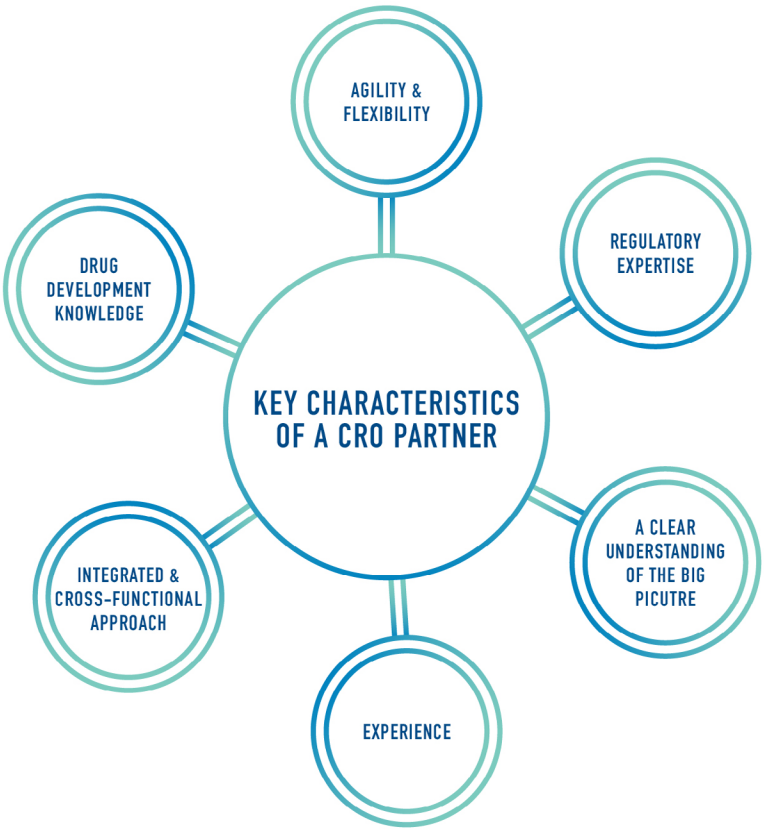
So while it's important to find the right strategic partner, emerging biotechs should always ensure to remember their own voice and make qualified decisions based on the input they receive.

KEY CHARACTERISTICS OF A CRO PARTNER

When looking for a partner, such as a CRO, to help strategize and execute your clinical development, biotechs should look for a number of key characteristics. With the right strategic CRO at its side, an emerging biotech can be made aware of risks or challenges along the way and adjust its strategy accordingly.

First, a biotech should ensure that the partner company has the necessary experience and knowledge to support it throughout preclinical and clinical drug development. It should also be agile and flexible and have the ability to react to unexpected hiccups in the process.

Experience can help here because many challenges can be foreseen and prevented if identified early enough. “It’s not only about identifying gaps, but it’s coming up with mitigation strategies to hopefully close these gaps,” Hansman adds.



This is best executed with an integrated and cross-functional team, which can have a clear understanding of the ‘big picture’ and provide a context in specific discussions for more strategic planning throughout the program.

Throughout the development process, but especially in later stages, an experienced partner can provide support when it comes to communicating with the regulatory authorities, abiding by regulatory guidelines, and putting together the right dossiers for regulatory feedback and approval.

“A partner interacts with the agency quite a bit and is familiar with a lot of their positions on common issues, such as those related to stability, toxicity, dose, or clinical trial design,” Hansman explains.

LOOKING INTO THE FUTURE

In recent years, the global life sciences industry has built up a powerful momentum. More and more cell and gene therapies are entering the market, targeting unmet medical needs and transforming how we treat diseases. Machine learning and artificial intelligence are shifting from being a novelty to becoming the norm. Personalized therapies and their polar opposite allogeneic therapies are steadily moving towards an inflection point. It is an exciting time for companies in the life sciences industry.

Globally, R&D spending is steadily increasing, with more and more drugs in clinical pipelines. In 2021, there were more than 6,000 products across all stages of drug development, representing a 68% increase since 2016. And the trend is expected to continue[8].

Oncology remains a key therapeutic focus area, holding 37% of the 2021 drug development pipeline[8]. Other focus areas are neurodegenerative disorders and infectious diseases as well as rare diseases, especially those related to the gastrointestinal tract.

In the future, experts expect to see an even greater focus on rare diseases and unmet medical needs. As an example, in the last three years, the number of gene, cell, and nucleotide therapies has more than doubled. However, many challenges, such as the high risk of failure, immense costs, and strategic complexity remain.

In short, companies within the life sciences industry continuously find themselves facing unknown, unexplored territories. But by building on experience and using established technologies and products as role models, biotech and pharma companies, together with their strategic partners, can work to bring novel therapies to patients in need.

In 2021, there were **6000** products across all stages of drug development, representing a **68% increase** since 2016

ABOUT MEDPACE

FULL-SERVICE CLINICAL DEVELOPMENT

Medpace is a top-10 CRO with the mission to accelerate the global development of safe and effective medical therapeutics. With a 30-year history of success working with the biotech industry, the company provides a therapeutically focused, integrated, global approach with a commitment to organic growth.

Medpace's culture and operating structure are purposely designed to accommodate efficient partnering, important for emerging biotechs with limited resources and sometimes limited experience. With the help of integrated, cross-functional teams, the company can ensure that it supports biotechs through every stage of drug development, from the moment they have identified their lead compound.

"We have extensive experience working with small and mid-size companies," says Heyrman. "We know how to be a seamless extension of a biotech's team so that we become one team working together towards that ultimate goal within its strategic plan. Clear communication, clarifying issues, ensuring decisions are being made, followed through, and communicated to the entire team—that's an expertise that exists within Medpace and that we like to extend to our colleagues on the biotechs' side as well."

Medpace is committed to **Making the Complex Seamless™** by providing uncompromising commitment to your clinical research and the highest level of ethical standards and performance, which translates to executing your trials on time, on budget.

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