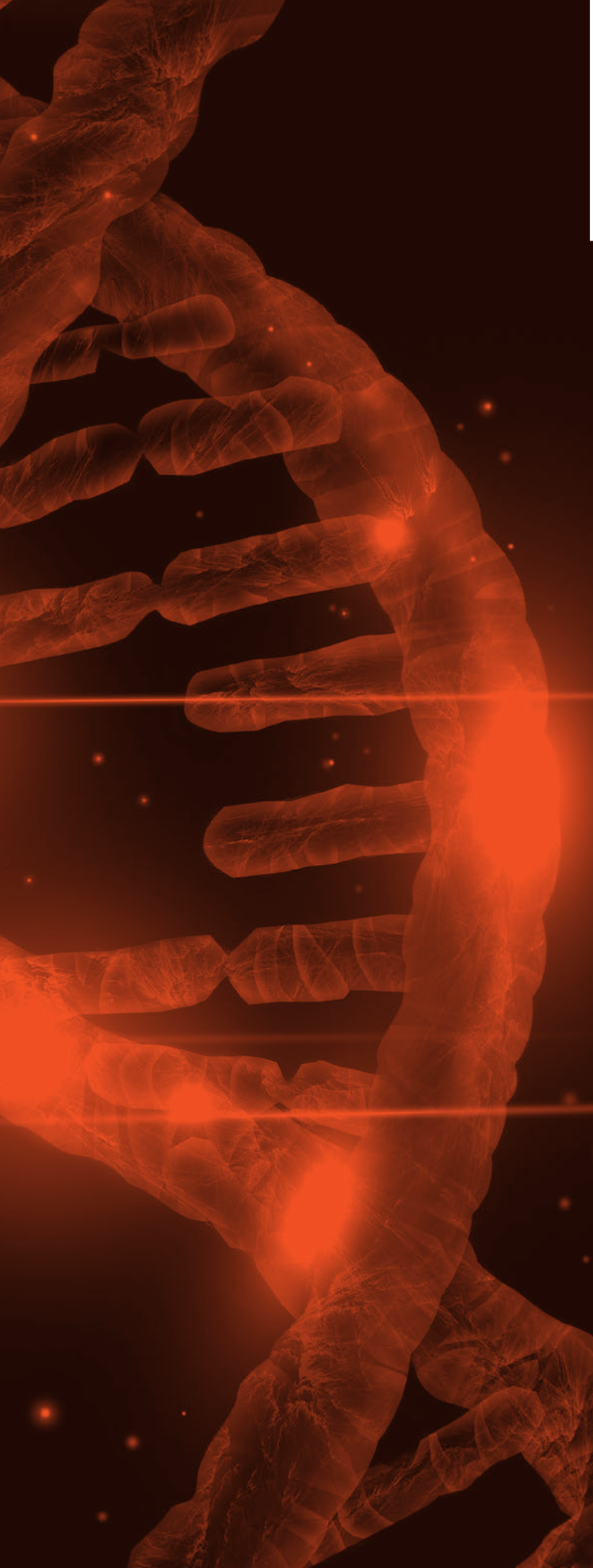
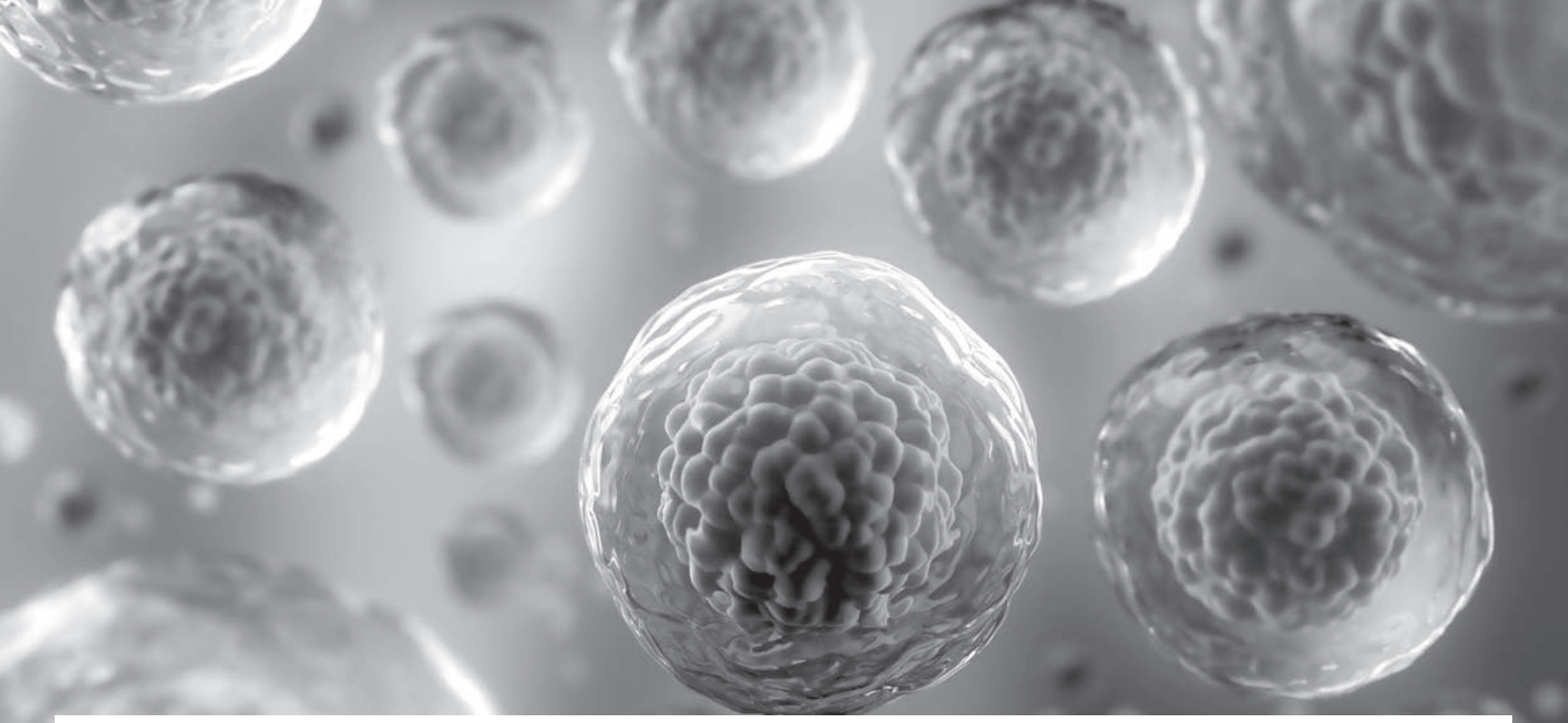


Syneos Health®
Insights Hub

Exploring an Expedited Regulatory Pathway for Cell and Gene Therapies

How the FDA's RMAT Designation Accelerates the Process



For many devastating diseases, regenerative medicine is the only hopeful chance at fighting them. This new frontier presents many challenges such as complex study design, patient populations with complicated considerations and distinct operational delivery requirements in the clinical trial setting. As a result, research in regenerative medicine or cell and gene therapy (CGT) is extremely arduous. Recognizing that this could hinder these important therapies reaching patients in a timely manner, the FDA established the **Regenerative Medicine Advanced Therapy designation (RMAT)** in 2017. Accelerating these processes means bringing therapies to patients that treat, modify, reverse or cure a serious or life-threatening disease or condition. Obtaining RMAT designation is far from simple, but its benefits are proving to be important success factors for accelerated commercialization. Understanding how and when to seek the designation should be the underpinning of evolving your regulatory pathway.

Accelerating these processes means bringing therapies to patients that treat, modify, reverse or cure a serious or life-threatening disease or condition.

Key Benefits of Regulatory Designations: RMAT

As with other regulatory designations, RMAT has the potential to accelerate the commercialization of therapies by:

- Optimizing your regulatory and clinical pathways through increased collaboration with the FDA;
- Increasing a therapy's visibility to the key stakeholders (including investor and medical stakeholders).

Critically, the threshold to obtain an RMAT designation is lower than for a Breakthrough Therapy Designation (BTD), while the benefits provided are similar.

An RMAT designation requires preliminary clinical evidence indicating that the drug has the potential to address unmet medical need for the disease or condition, while a BTD designation requires evidence indicating substantial improvement over available therapies.

Optimizing Regulatory and Clinical Pathways

Typically sponsors with an RMAT designation can expect a higher level of engagement with the FDA, with interactions becoming more of a problem-solving partnership compared to traditional interactions. Sponsors can then leverage the insights gained to optimize their regulatory and clinical pathways.

Other benefits of this partnership-type engagement with the FDA include:

- When granted RMAT designation, all meetings with FDA will be scheduled as Type B meetings;
- Feedback on the inclusion of surrogate or intermediate endpoints;
- Priority review likely to be granted;
- Early exposure to stakeholders from the Center for Biologics Evaluation and Research;
- Engagement with Senior Staff and Subject Matter Experts.

Increasing a Therapy's Visibility

When it comes to market optimization, the RMAT designation can add value to the company. It signals to investors that the regulatory pathway and studies will be enhanced by this designation due to the higher level of engagement with the FDA.

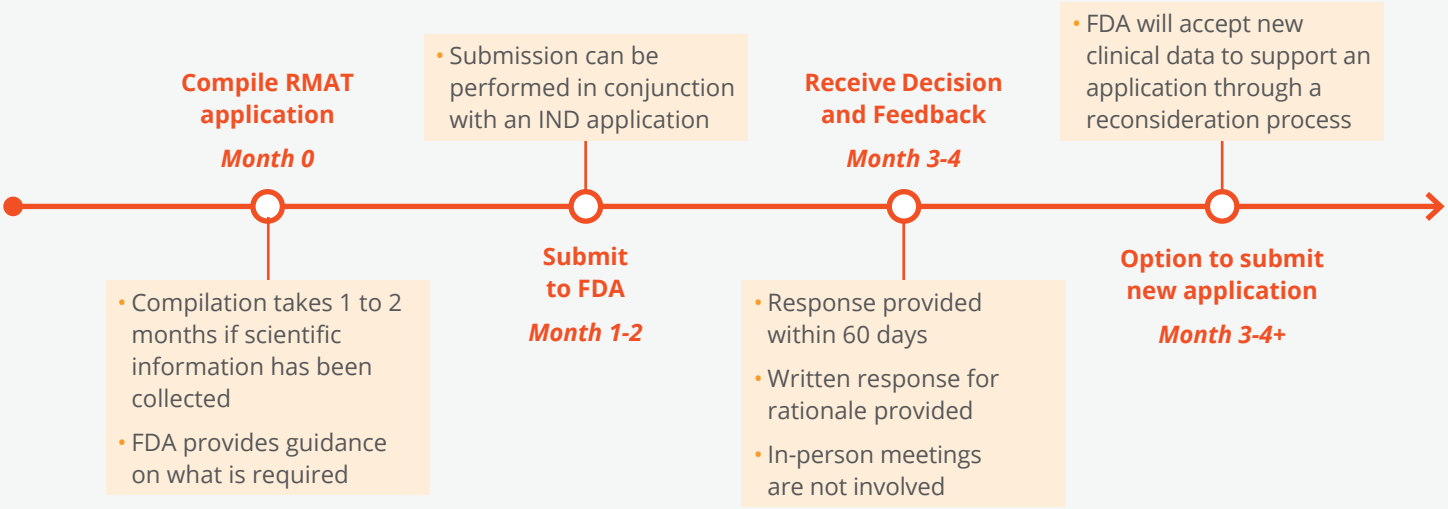
Meeting the Threshold of RMAT Designation

Before embarking on applying for an RMAT designation, biopharma companies need to understand that there is a significant time investment and need for preliminary clinical evidence. The application for RMAT can be challenging, with 31% of applications on average being successful since 2017. This is in comparison to the 40% success rate for BTD applications. An important distinction to make, however, is that the RMAT designation does not require evidence of a substantial improvement over available therapies. Before you approach the designation process you need to demonstrate that your therapy:

- treats, modifies, reverses or cures a serious or life-threatening disease or condition;
- has the potential to address unmet medical needs for the disease or condition (as indicated by preliminary clinical evidence).

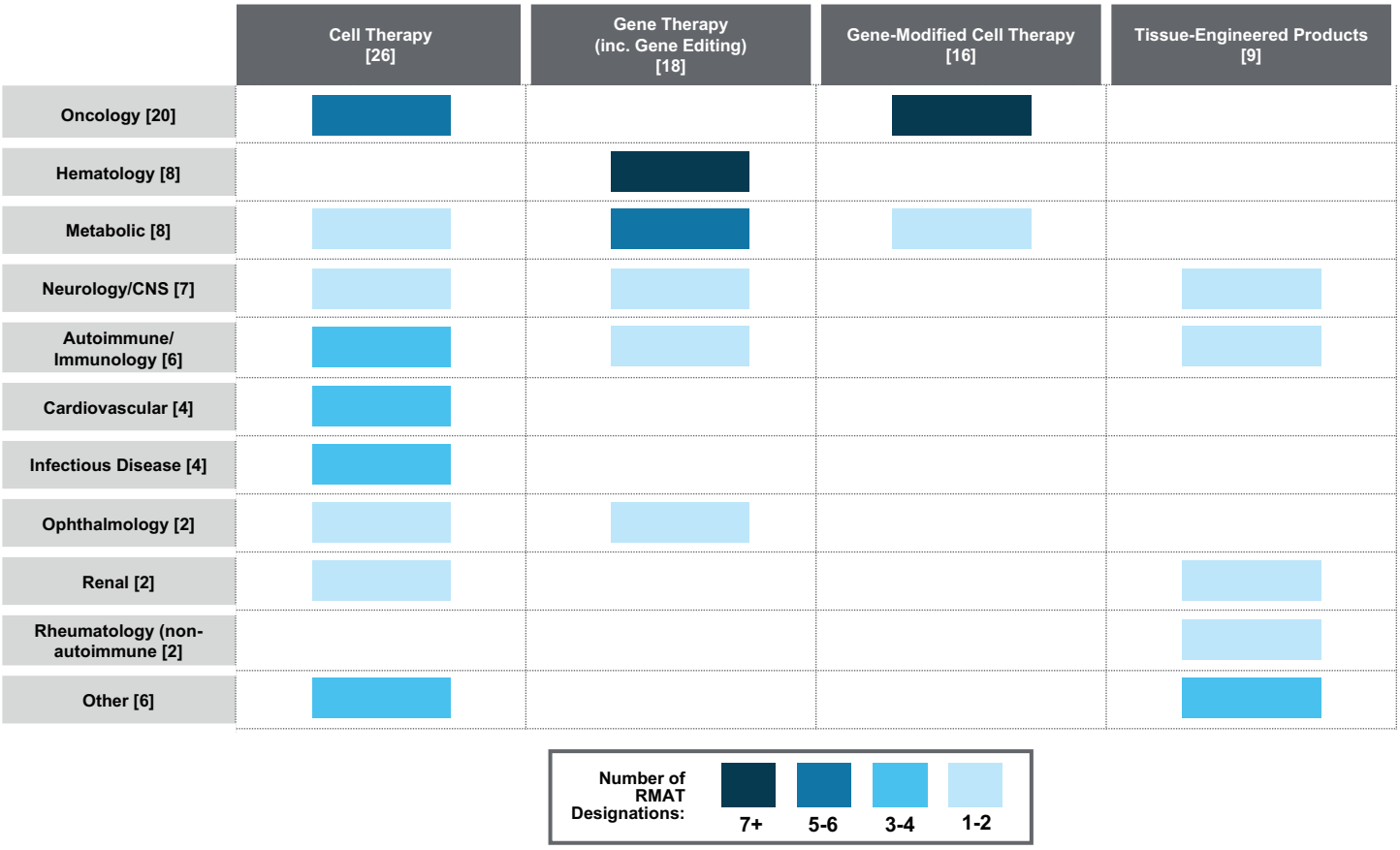
You should plan to allow three to four months (Fig. 1) to generate the required clinical and product data for the actual application process that provides compelling early signs of efficacy and a clearly demonstrated unmet need. Successful applications typically also focus on Chemistry Management and Controls (CMC), as an applicant will need to ascertain that potential necessary modifications to drug product do not alter the safety of performance relative to the drug product used to generate the initial clinical data. The more time spent up front on making the application as well written and compelling as possible, the shorter the application process will be.

Figure 1. Typical Timeline of RMAT Application Process



Since its inception, the FDA has designated 77 companies with RMAT across a diverse range of platforms and indications (Fig. 2).

Figure 2. Current RMAT Designations



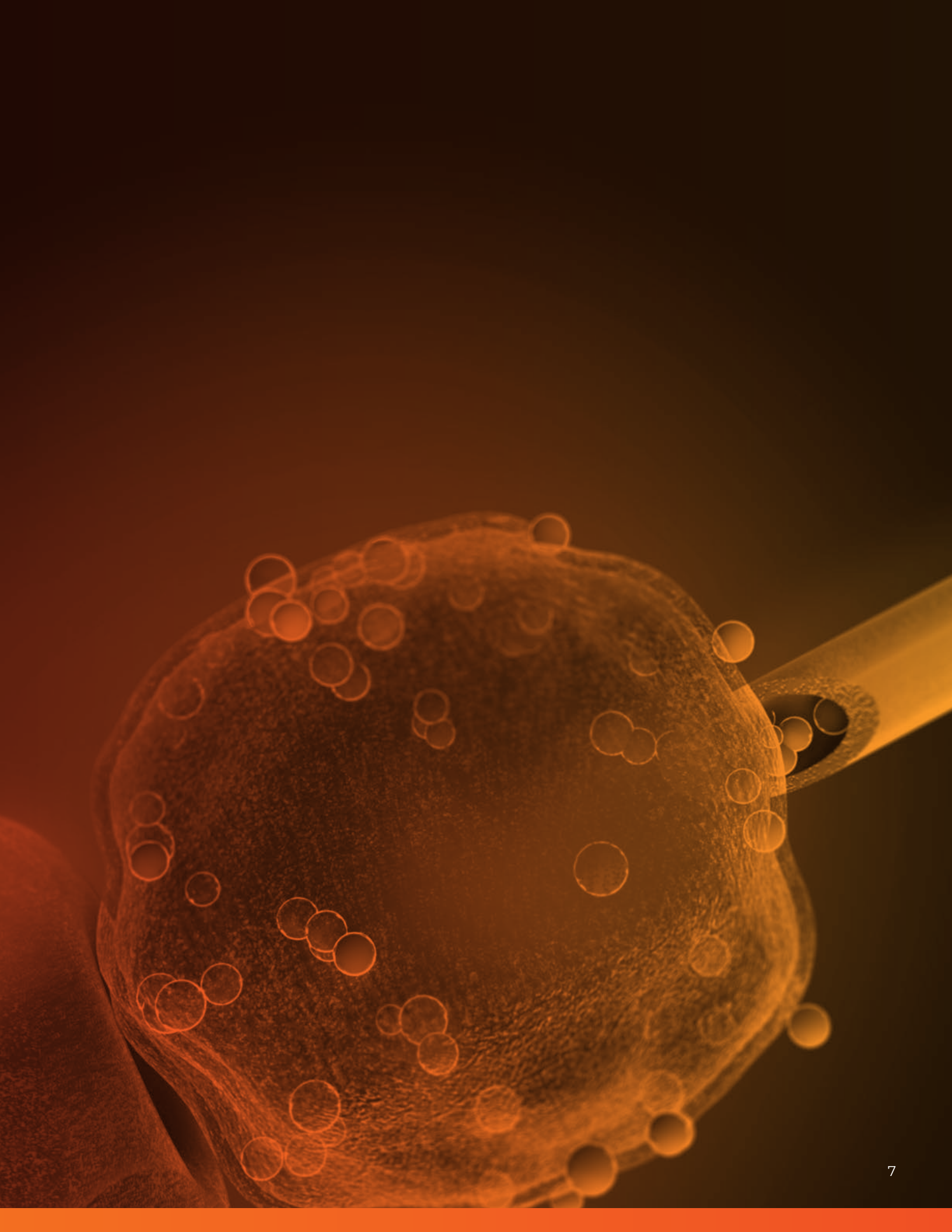
Navigating the Expedited Path

Any new path can be daunting for a company seeking to commercialize its therapy. For a company with one that falls in the regenerative medicine category, the process can seem even more so. However, if your asset meets the basic criteria for RMAT, investing the time to apply for it, and doing so in the right way, can help add value to your asset and increase interaction with the FDA as you move through the regulatory process. When seeking RMAT designation, it's important to ensure customers meet the basic criteria and then design pre-clinical testing and clinical trials with an eye toward meeting the designation requirements. Assessing phase I through phase II clinical data as it is developed will help customers determine whether to greenlight the application process once they meet the threshold for clinical data.

Syneos Health also conducts a thorough RMAT submission readiness assessment and works with customers on planning for clinical and regulatory aspects of the process, then helps customers prepare their final submission to the FDA.

An Opportunity to Enhance Your Asset

Since it is still relatively new, the RMAT designation and its benefits aren't widely known or understood. The specific scientific and medical implications of the therapy, the specific therapeutic area and regulatory requirements are all key considerations when bringing a regenerative medicine to market. This includes the RMAT designation, which can accelerate the process. Incorporating the additional considerations for the designation is integral to harnessing its advantages and accelerating a medicine for a devastating illness to reach a patient sooner. While not widely known or understood, RMAT is a means for a company with an asset in regenerative medicine to accelerate the process and provide the therapy to the patient safely and effectively.



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About the Syneos Health Insights Hub

The Syneos Health Insights Hub generates future-focused, actionable insights to help biopharmaceutical companies better execute and succeed in a constantly evolving environment. Driven by dynamic research, our perspectives are informed by our insights-driven product development model and focused on real answers to customer challenges to help guide decision making and investment.

About Syneos Health

Syneos Health® (Nasdaq:SYNH) is the only fully integrated biopharmaceutical solutions organization purpose-built to accelerate customer success. We lead with a product development mindset, strategically blending clinical development, medical affairs and commercial capabilities to address modern market realities.

Together we share insights, use the latest technologies and apply advanced business practices to speed our customers' delivery of important therapies to patients. We support a diverse, equitable and inclusive culture.

To learn more about how we are **Shortening the distance from lab to life®**, visit syneoshealth.com or subscribe to our podcast.

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