Are Cell and Gene Therapy programs a better bet?

Compared to traditional drug development programs, do durable cell and gene therapy (CGT) programs experience higher or lower clinical success rates? Estimating the Probability of Technical and Regulatory Success (PTRS) is a key factor affecting a drug developer's decision to initiate human clinical trials. A higher Likelihood of Approval from Phase I (LoA) increases a program's attractiveness to clinicians, developers, and investors alike. This comparative analysis suggests durable CGTs for orphan diseases and hematological cancers are 2-3.5X more likely to succeed than other therapeutic modalities for similar conditions or compared to the entire drug pipeline.

RESEARCH BRIEF

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Securing clinical development funding always proves challenging. In 2023, durable cell and gene therapies have achieved over a dozen product-indication approvals from the FDA with hundreds in development[1]. With success has also come questions as the field matures. Investors, in optimizing their portfolio strategies, seek additional signals regarding the relative attractiveness of CGT.

APPROACH

We compared the clinical trial success rates and overall likelihood of approval from the NEWDIGS FoCUS Pipeline Analysis Model (PAM)[2] for durable cell and gene therapies to recently published BIO[3] and IQVIA[4] estimates based on clinical trials from all therapeutic modalities. The FoCUS PAM model analyzes all CGT trials reported to clinicaltrials.gov from 1988 through end 2020. Our comparative analysis selected the BIO and IQVIA estimates over possible academic alternatives to ensure comparison to datasets that also extended through at least 2020 (Table 1). We compared CGT likelihood of approval from Phase I, as well as individual clinical development phase success rates, to the more general drug pipeline. All sources similarly grouped Ph I/II trials and Phase II/III trials into Phase II and Phase III respectively, facilitating comparison. BIO also reported estimates by major disease areas, which allowed more direct comparisons to oncology and rare diseases which dominate the CGT pipeline.

Key takeaways

CAR-T/TCR therapies for blood cancers are 3X as likely to be approved when entering Phase I as the average oncology drug and over 2X as likely as the average hematological oncology drug.

Orphan gene therapies are 2 – 3.5X as likely to be approved when entering Phase I as the average drug in clinical trials, outperforming in every clinical development phase.

Orphan gene therapies are 2X as likely to be approved when entering Phase I as the average drug in similar therapeutic areas*, outperforming in every phase.

	PAM	BIO	IQVIA	Wong et al (MIT)[5]	DiMasi (Tufts)[6]
Data sources	clinicaltrials.gov	Biomedtracker Informa	IQVIA Pipeline Intelligence	TrialTrove & PharmaProjects by Citeline	50 biopharma
Trial data date range	1988-end 2020	Jan 2011-Nov 2020	2010-2022	2000-Oct 2015 (16 years)	1993-2009 (17 years)

Table 1. Summary of industry and academia references with published clinical drug development success rates estimates

*Therapeutic areas considered: hematology, autoimmune, metabolic, neurology, and ophthalmology

Oncology

CAR-T/TCR therapies for hematological oncology (17.2% LoA) are 3.2 times as likely to be approved when entering Phase I compared to the average oncology drug (5.3% LoA; Figure 1 left panel). Despite lower success in Phase I, hematologic CAR-T/TCR therapies candidates then go on to outperform the average oncology drug in every subsequent clinical development phase.

Hematologic CAR-T/TCR therapies repeated this pattern of lower Phase I success followed by higher subsequent success, in a more 'head-to-head' comparison to hematological oncology drugs. Upon entering the clinic, CAR-T/TCR therapies see more than double (2.3 times; Figure 1 right panel) the likelihood of approval upon entering Phase I.

Figure 1

Left: Comparison of likelihood of approval and phase success rates for hematological CAR-T/TCR therapies (PAM estimates) and all oncology drugs (BIO estimates).

Right: Comparison of likelihood of approval and phase success rates for hematological CAR-T/TCR therapies (PAM estimates) and hematological oncology drugs (BIO estimates). NDA/BLA = regulatory review phase.

Rare diseases

CGTs for orphan gene therapies (27.6% LoA) are 2 to 3.5 times as likely to be approved when they enter Phase I clinical development as the average drug (BIO 7.9% LoA; IQVIA 13.2% LoA; Figure 2). Compared to the all modalities estimates from either BIO or IQVIA, orphan gene therapies have better success rates in every clinical development phase.

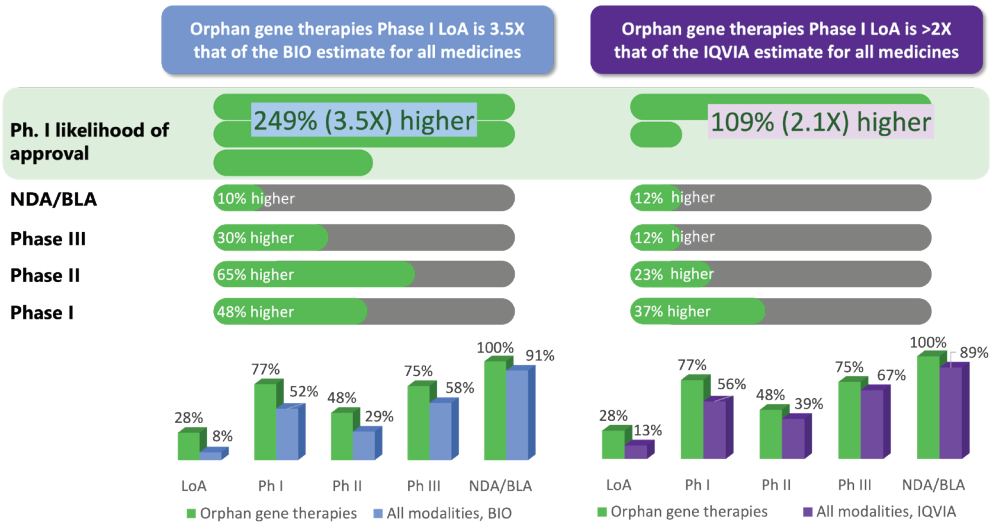

Figure 2

Comparing Likelihood of Approval and phase-by-phase success rates for Orphan gene therapies (PAM estimates) compared to all modalities (Left: BIO estimates; Right: IQVIA estimates). NDA/BLA = regulatory review phase.

Beyond oncology, CGTs concentrate in a few therapeutic areas: hematology, autoimmune, metabolic, neurology, and ophthalmology. To approximate a "head-to-head" comparison we used the BIO therapeutic area estimates to calculate simple (unweighted) composite success rates for that therapeutic area subset. CGT orphan gene therapies are still more than twice as likely to be approved as the average drug in similar therapeutic areas (28 % LoA / 13% LoA = 2.2X) and outperform in every phase of the clinical development process (Figure 3).

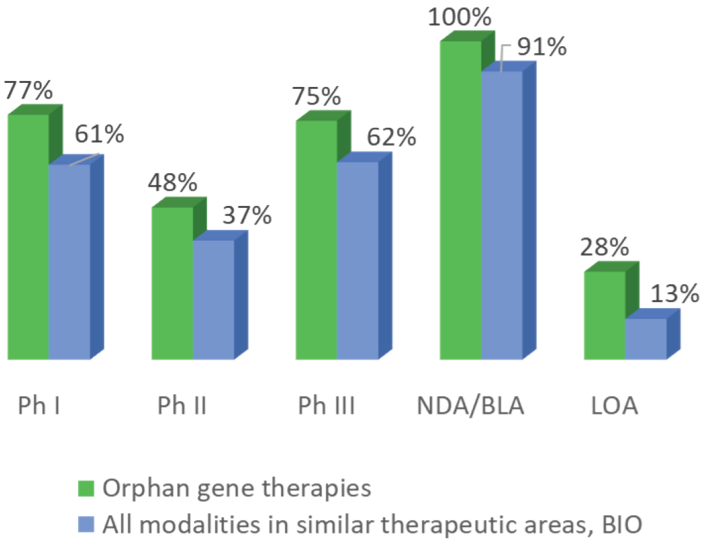

Figure 3. Orphan gene therapies are more than twice as likely to be approved as the average drug in similar therapeutic areas, outperforming in every phase

CAUTIONS

This analysis compares historical success rates for completed clinical trials whose next step for the candidate therapeutic (progression or not) is known. These may not represent current or future trials.

Some CGT areas were not yet sufficiently mature to be included in the analysis such as cell therapies for solid tumors.

As with most drug pipeline analyses, we did not perform an age cohort analysis – these results may therefore exhibit some unknown level of success bias.

The PAM model success rates contain all clinicaltrials.gov reported CGT results back to 1988 with possibly lower success rates in early years, which may make PAM results more conservative (lower) than the estimates from other sources.

The BIO and IQVIA success rates include CGT programs, which if excluded, would lower the estimate for a non-CGT success rate and so further increase the CGT relative performance.

IMPLICATIONS

Taken together, our research suggests that durable CGT programs for rare orphan conditions and CAR-T/TCR therapies for hematological cancers have higher success once they enter the clinic compared to the combined pipeline of all therapies. This is consistent for comparisons to:

- Likelihood of approval from Phase 1, for all therapeutic programs
- Programs in the same therapeutic areas
- Every development phase, except Phase 1 for CAR-Ts

These results illustrate the power of compounding incremental success across nearly every phase for all CGTs. They suggest that drug developers and investors should consider the full likelihood of approval when comparing their options, not only the immediate next clinical milestone.

Durable cell and gene therapies are demonstrating transformative patient impact; their clinical success rates may also transform drug development and associated financial returns.

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ABOUT FOCUS

The NEWDIGS consortium FoCUS Project (Financing and Reimbursement of Cures in the US) seeks to collaboratively address the need for new, innovative financing and reimbursement models for durable and curable therapies that ensure patient access and sustainability for all stakeholders. Our mission is to deliver an understanding of financial challenges created by these therapies leading to system-wide, implementable precision financing models. This multi-stakeholder effort gathers developers, providers, regulators, patient advocacy groups, payers from all segments of the US healthcare system, and academics working in healthcare policy, financing, and reimbursement in this endeavor.

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