Funding Triggers: Therapeutics & Drug Development

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Bringing a new medicine to market is one of the most challenging journeys in biotech.

The process typically spans 10–15 years[i], with investment that can reach into the billions. A Deloitte study based on 20 top global biopharma companies estimated an average investment of $2.23 billion per drug ("or asset") in 2024[ii], while a study published in JAMA Network Open based on 2014-2019 R&D costs from drugs approved by the FDA in 2019, illustrated the extreme variability. It estimated a median cost of $708 million and a mean of $1.31 billion after adjusting for failures and the cost of capital[iii].

Success rates are modest; ~6.7% of drug development programs entering Phase I clinical trials gained approval according to a study of 2014-2023 data with significant variances depending on therapy focus – from 4.5% for respiratory to 19.1% for hematology (Citeline). This reflects a decline from historical rates in earlier cohorts as the industry pursues more complex therapeutic approaches[iv]. However, the impact on patients and society can be transformative. A multi-asset approach can help diversify risk in response to low success rates, but it can also introduce complexity and resource challenges[v]. AI, data, and computing power are rapidly changing the development landscape with the potential to shorten timeframes, reduce costs and ultimately bring more effective therapeutics into the world[vi].

Modest Success Rates: ≅7%

Definition & Scope: Development of new medicines and therapeutic products intended to treat, prevent or modify disease biology, requiring regulatory approval and advancement through clinical development pathways. This includes therapeutic innovations using biological mechanisms, advanced modalities, engineered approaches and / or novel chemistry - targeting areas such as oncology, neurology, immunology, cardiovascular and metabolic disease, infectious disease, rare diseases, and other areas of unmet medical need.

Core Technologies: Small molecules, biologics, monoclonal antibodies, cell and gene therapies, RNA therapeutics (including mRNA platforms), radiopharmaceuticals, antibody-drug conjugates (ADCs), CAR-T and TCR therapies, CRISPR/Cas9 gene editing, targeted protein degraders (PROTACs), and AI-driven drug discovery platforms.

Typical Startup Profile: Often originates as a university spinout or from biotech innovation labs, through licensed IP or proprietary research[vii]. Founders are typically PhD/MD scientists with deep domain expertise. Founders, whether repeat or first-time, frequently leverage biotech venture studios, incubators, accelerators, business plan competitions, and innovation labs to support translating research into investable startups. Therapeutic/drug development ventures are highly capital intensive with long development timelines and often remain pre-revenue for many years or get acquired before commercialization[viii]. To navigate clinical and regulatory milestones and form strategic partnerships, biotech teams often combine strong scientific expertise with leaders who have industry experience. Computing / modeling expertise is increasingly relevant and key for platform drug ventures.

Market Notes (Mar 26): Biotech holds a significant share of global VC funding, though overall the funding environment was challenging in 2025 but a cautiously more positive outlook has been noted into the beginning of 2026[ix].Funding concentration was observed with mega-rounds for high-profile AI-leveraged drug discovery platforms and some later-stage ventures, while early-stage venture activity and IPOs were subdued[x].

Policy shifts at the NIH and regulatory changes at the FDA are contributing to an evolving development environment[xi]. **High regulatory risk and large capital needs, clear milestones critical and early partnerships influential.** The Deloitte study estimated the internal return on investment (IRR) on late-stage pipeline for top 20 biopharma companies to be 5.9% in 2024, but it is worth noting that GLP-1 therapies (obesity/diabetes drugs) had a significant impact. Excluding this asset class, the estimated IRR dropped to 3.8%[xii]. **This illustrates how a single high-performing therapeutic category can skew investor returns and influence the flow of capital.**

Exit Pathways: M&A is currently a dominant exit pathway. Large pharmaceutical companies often acquire targeted, promising startups around or after strong Phase II clinical data to reduce late-stage development risk and accelerate pipeline growth. Licensing agreements are also common, particularly for targeted platform technologies or early-stage assets[xiii]. IPOs typically favor companies with late-stage assets and validated clinical data. Given the significant capital requirements and long timelines, strategic partnerships and M&A tend to be the most frequent outcomes for promising ventures.[xiv]

Critical Milestone - IND Clearance & Start of Phase I: The Investigational New Drug (IND) application becoming effective (absent a clinical hold by the FDA) signals a key transition point, allowing Phase I clinical trials to begin. This milestone moves a program from preclinical promise to human testing, often increasing investor confidence and the likelihood of deeper pharma engagement.[xv]

Breakthrough Therapy Designation: FDA Breakthrough Therapy designation can significantly accelerate development timelines and regulatory review, while boosting valuation by signaling strong clinical potential. An analysis by Jefferies evaluated 599 breakthrough therapy designations granted from 2013 through early 2025. For the 2013-2022 subset, 72% ultimately achieved FDA approval and an additional 13% were awaiting decisions.[xvi]

Keep in Mind: Approximately 38-40% of FDA Breakthrough Therapy designation requests are granted. Among all FDA drug approvals in recent years, about 25-36% had been previously granted Breakthrough Therapy status (multi-year average; individual years have ranged from approximately 16% to 41%), underscoring the selectivity and strategic role of the designation in accelerating promising therapies.

Drug Development Process

For a new drug or therapeutic to reach patients in the U.S., it must generate sufficient evidence of safety, efficacy, and quality to progress through successive stages of development and regulatory review. The U.S. FDA describes this journey at a high level as a sequence of stages, from discovery and preclinical research through clinical development, regulatory review, and post-marketing surveillance, as summarized in the table below[xvii]. The process is neither uniform nor strictly linear. Each stage contains multiple technical, regulatory, and strategic decision gates, and requirements vary significantly by modality, therapeutic area, regulatory designation, and program-specific risk profile. Study design, milestone definitions, timelines, and capital intensity are therefore highly individualized, with advancement contingent on the strength and sufficiency of the evidence generated at each go/no-go inflection point.

Drug Development Continuum

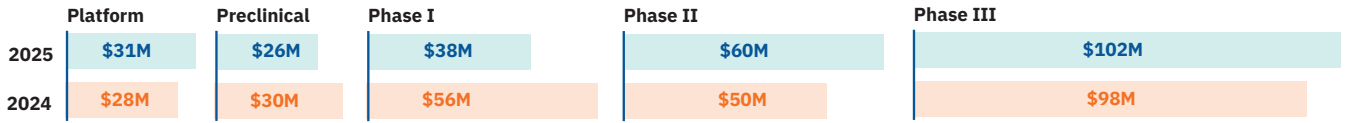
Phase	Discovery =>	Preclinical Research =>	Clinical Entry (Phase I) =>	Clinical Expansion (Phase II) =>	Clinical Completion (Phase III)	Regulatory Review & Approval =>	Post-Marketing Surveillance
Typical key activities	Target identification & validation; assay validation; hit-to-lead screening; lead optimization	Nonclinical efficacy; ADME; toxicology; CMC, IND-enabling studies	First-in-human dosing; safety, PK/PD; dose escalation	Dose optimization; preliminary efficacy; continued safety evaluation; biomarker refinement where applicable	Confirmatory efficacy and safety; larger scale trials	FDA review; advisory committee review (if appl.); label negotiations; manufacturing inspections etc.	Long-term safety and effectiveness; Phase IV studies if required
Typical ending milestone – go/no-go gateway to next phase	Lead candidate identified and sufficiently characterized to advance into preclinical dev	IND submitted and becomes effective (no clinical hold), enabling initiation of clinical trials.	Safety profile and dose range established; decision on Phase II progression	Evidence of efficacy and dose selection sufficient to justify Phase III dev; decision on Phase III progression	Data sufficient for NDA/BLA submission; decision to seek reg. approval	Reg. approval granted; go/no-go for market launch	Ongoing monitoring; informs label changes or program continuation

Regulatory Pathways Beyond the U.S. FDA: Overseas regulatory pathways are sometimes pursued by U.S. biotech startups depending on market access, strategic considerations, and financial implications. These include pathways governed by EMA (EU), PMDA (Japan), MHRA (UK), and NMPA (China).

Typical Funding Stages & Funders

Funding stages are not rigid. For example, looking at Labiotech's 2024 funding tracker, you can see that global seed rounds can occur across a range of development stages, including discovery, preclinical, and early clinical phases. Capital ranges vary widely and can be shaped by set-up factors (notably founders), modality (small molecules, biologics, cell/gene therapy), platform vs. asset focused, indication, endpoints, geography, and so on.

JP Morgan (fueled by DealForma)[xviii] calculates median venture funding rounds by company stage:



2024 biotech rounds include large/mega rounds for example at Seed - one of $63M and another of $100M and at Series A - two rounds of $400M and one round of $300M.

	Pre-Seed	Seed	Series A	Series B
	Source: Esinli Capital[xix]	Source: Labiotech 2024 Biotech Funding Tracker[xx]		
Ranges	~$0.5M–$1M+	$4.6M - $100M	$8.9M - $400M	$9M - $260M
Median		$13M	$57M	$85M
Typical Funding Sources	University TTOs; Grants (e.g. SBIR/STTR Phase I); philanthropic foundations; patient advocacy and disease- specific foundations; angels; F&F; incubators; venture creation firms and platforms	Seed biotech VC funds; family offices; grants (e.g. SBIR/STTR Phase I); BARDA/government programs (primarily health security/pandemic preparedness countermeasures); patient advocacy and disease-specific foundations; translational grants; nontraditional/self- funding (e.g. AI platform revenue); angel syndicates and biotech angel networks; early partnerships with translational research orgs or pharma scouts	Biotech /healthcare VCs; specialized life sciences funds; corporate venture; pharma option/licensing; milestone-based partnerships; grants (e.g. SBIR/STTR Phase II)	Growth-stage VCs; crossover investors; pharma venture arms; royalty/structured finance; larger institutional funds looking for differentiation and clinical proof points

NOTE: M=$ Millions

Patient Advocacy & Venture Philanthropy: Disease-specific foundations, venture philanthropy, and impact investors are playing a very important role in startup funding for therapeutics R&D. Some organizations have non-dilutive programs, while others have funds to invest directly in early-stage therapeutics. Importantly, some institutes offer valuable resources such as shared infrastructure, data, expert advice, etc. In addition, **FasterCures' TRAIN** network connects over 180 such foundations.

Grants and Awards: Non-dilutive awards can not only fund R&D without giving up equity, but they can also enable collaboration, help de-risk projects, and signal validation to private investors. Some programs can be significant, sometimes into the millions, such as BARDA contracts.

Funding Triggers: Peeling the Risk Layers of the Onion

Funding rounds serve to fund the activities that bring the company to its next inflection point and in doing so off-loads or mitigates specific risks. These risks can be across any number of the key domains: strategy & execution (team and governance), scientific & development, IP, regulatory & clinical, market & commercialization, manufacturing & operating business model.

By achieving these value-creating milestones, the company, in theory, attracts the next stage funders and secures the opportunity to progress to the next stage of de-risking activities. The analogy of peeling the onion (Marc Andreessen & Andy Rachleff) has been used to illustrate this approach of systemically removing or reducing specific risks, layer by layer.

Designing milestones backwards from the next funding round are particularly important in biotech where capital requirements are high and so too is the risk of future financing. Thus, at each stage of funding **two starting questions are:**

1. What justifies funding at this stage? **(accomplished milestones)**
2. What can be achieved with the proposed funding? (execution of the plan to deliver the **next set of milestones** that should be designed with anticipated requirements in mind to unlock the next stage of funding).

Figuring out **the right quantum of proposed funding** can thus take into account:

1. The risk / reward equation given that valuation and risk are inversely correlated;
2. Resources needed to deliver the plan with cushion for the likelihood of delays and unforeseen challenges; and
3. The current and anticipated funding climate (ever-evolving – we appreciate it is difficult to forecast).

When the realistic go-to market plan is known and with line of sight of what milestones future investors may require, the plan can be devised backwards and can inform partnership and collaboration strategy, tests and trial design, number of products to be pursued, at what time, hiring plan and so on.

At the time of a funding round, the set of milestones you propose to be funded may match the set of milestones you plan to show your future investors at the next stage. **(See discussion with V. Agarwala, MD/PhD, Andreessen Horowitz; https://www.youtube.com/watch?v=t1AHFTCj4yo).**

In reality, plans rarely, if ever, pan out exactly as initially drafted. Timelines are long in therapeutics and drug development, and uncertainty is inherent. It is still key to pre-plan and within those plans to set triggers for continuing, pausing, resetting, pivoting or stopping. This brings us to the trope of **"navigating the idea maze,"**[xxii] (a concept introduced by Balaji Srinivasan and subsequently adopted by Marc Andreessen). Andreessen has recommended to "pre-plan possible futures" and then adjust daily as new information arises. The emphasis is on course-correcting and evolving vs. impulsive reactions. Key qualities to cultivate are resilience and openness with your trusted advisors.

Moving Valleys of Death: With typically high capital requirements, long routes to commercialization, and translational challenges to navigate, several valleys of death in biotech have been documented. Systemic funding gaps arise when risks are perceived as too great for traditional investors. The gaps are exacerbated in periods of capital scarcity. BiopharmIQ data (see ix) shows early-stage funding fell 10–20% in 2025, even as later-stage capital remained robust. Founders must plan carefully and not assume that Series A will immediately follow a Seed round. This circles back to the importance of venture philanthropy and government-backed funding.

What are the specific milestones?

The Milestone Matrix*

	Pre-Seed	Seed	Series A	Series B
What are key risks mitigated, and the milestones achieved that unlock this round?	• Is the biology and target validated enough to form a company? • Do we have defensible IP and FTO? • What proof of concept data unlocks seed funding?	• What preclinical data most reduces scientific risk? • Is the regulatory path to IND credible? • What team and infrastructure are needed for Series A?	• What IND-enabling work gets us to the clinic? • What plan de-risks clinical exclusion? • What early clinical data unlocks the next round?	• What clinical results validate the asset? • What partnerships or licenses should begin now? • What manufacturing and marketing readiness is required next?
What will you achieve with this funding? What risks will be reduced or eliminated and what milestones will be achieved?	• What proof of concept will we share? • What IP will we secure? • What early risks will we face? • Is there a credible path to future adoption, and who helps us get there? • Focus: *Use partnerships for validation, not scale*	• What preclinical milestones will our venture reach? • What key scientific risks will be reduced? • What evidence and relationships make this partnerable? • Focus: *Partnerships shift from validation → execution + optionality*	• What milestone gets us into clinic? • What regulatory risks will be reduced? • What data validates the program? • What proves this will be adopted and who will commercialize it? • Focus: *Partnerships become strategic (path to exit)*	• What clinical proof will we show? • What development risks will be reduced? • What partnerships and options will this unlock?
Typical Development Stage	Discovery / early preclinical	Preclinical development	IND filing → Phase I start	Phase I completion or Phase II entry
Key Trigger	Biology validated; IP secured Investor question: Is it real?	Lead candidate selected; IND-enabling plan Investor question: Is it investable?	IND cleared; first-in-human trial begins Investor question: Is it partnerable/ acquirable?	Safety + early clinical signal Investor question: Is it proven and scalable?
Sample Milestone 1 (what investors will want to see)	Target biology validated in disease models	Lead drug candidate selected	IND cleared; Phase I trial initiated	Phase I safety and dose established
Sample milestone 2 (what investors will want to see)	Core therapeutic IP secured	IND-enabling development plan defined	Clinical program and CRO infrastructure established	Early clinical efficacy signal demonstrated

**Despite its linear structure, effective venture planning requires early, parallel development of IP and CMC strategies, aligned to milestones, to systematically de-risk downstream clinical, regulatory, and commercial outcomes.*

There is no universal mapping of milestones to funding stages in therapeutics startups or perhaps in any startup. **The specific milestones are specific to the startup.** There is great variability in size of rounds, types of innovations and therapeutic modalities, and requirements at different stages etc. What is consistent is that investors expect to see forward progress, ultimately towards the patient, and that each funding event should be justified by a reduction in risk.

Each startup is thus tasked with **mapping their own milestones.** Hopefully, useful feedback from prospective funders for both your current and future rounds can be helpful.

To get started in the process, we have listed some preliminary questions below. Can you add to them for the stage of your startup and where you want your plan to take your venture for the next value-creating milestones?

	Sample Questions Before Mapping
Team & Execution	• Do you have the scientific and technical caliber and the execution capacity necessary to deliver the plan to reach the next milestone? • Where are our capability gaps relative to the next milestone? • Is governance structured to handle difficult decisions? • Is the team prepared to cope with uncertainty and to collaborate? • What SAB and KOLs make-up and level of input makes sense at what time?
Science & Technology	• Is the biology and the science understood? What validation do you have now and what are you trying to de-risk at every stage? • What specific dataset would materially reduce that uncertainty? • Do you have access to the right technologies and expertise? • What is your competitive advantage?
Regulatory & Clinical	• What does the regulator need to see before the next inflection point? • Are endpoints, biomarkers, and indication choice aligned with eventual approval strategy? • Is the data reproducible, externally validated, and decision-grade?
IP	• Is FTO confirmed in your core indication? • What is your IP strategy and patent position? • If a competitor emerged tomorrow, what protects you?

	Sample Questions Before Mapping
Pre-commercial, commercial & Market	• What is the translational research roadmap? • Is the unmet need urgent and economically meaningful? • Is your target product profile differentiated in a clinically meaningful way? • What evidence or event would convince a strategic partner to engage? • At what stage do you work on an adoption plan?
Manufacturing & Operating Model	• What time is the right time to begin CMC planning? • What are your collaboration and partnership strategies and how do they impact other plans, design of trials, data packages, pilots etc.?
Finance	• Are the budget and time-lines justifiable and credible at each stage? • How much capital is required to reach that inflection point with appropriate cushion? • If funding markets tighten, what is the contingency plan? • Are the appropriate accountability, KPI planning and controls in place?

Some common terms:

Seed Round: Generally, the first raise with an institutional investor, e.g. VC. Can be raised over several rounds, covering varying lengths of capital requirements, typically 18-24 months.[xxiii]

Series A: The next raise after a seed round, usually much larger in size and which meets the milestones for investors at this stage – still considered early stage.

Series B-D: Follow-on rounds with typically progressively larger sizes.[xxiiv]

Dilution: Founders should be aware that each funding round **typically dilutes existing ownership.** By the time a startup reaches Series B or beyond, the original founders often hold a much smaller fraction of the company. Careful planning of milestone delivery can help with negotiation.

Therapeutics has produced only about ~20 unicorns globally in the past five years, making it one of the rarest unicorn categories in venture capital, despite attracting large total investment.

Venture Technology and Business Level Readiness (TRL and BRL)

TRL is a well-recognized framework, widely used by some government agencies, academic and research institutes, industry and by some private investors, though adoption can vary across the industry.

BRL is an emerging, non-standardized framework for assessing business and commercial readiness and ranges can be approximate. It reflects operational, regulatory, and market preparedness, but **does not substitute for clinical evidence or reduce scientific risk.**

Why TRL and BRL Matter for De-Risking a Biotech Startup (through the Founder's Lens)

- **They separate scientific promise from investable readiness.**
  Many first-time founders overemphasize the importance of scientific novelty. TRL provides an objective signal of technical and clinical de-risking. At the same time, BRL exposes gaps in regulatory strategy, capital planning, and commercialization - areas where first-time teams statistically struggle relative to repeat founders.
- **They align the funding strategy with realistic milestones.**
  Empirical venture data show that biotech capital is released against risk reduction, not a founder's vision. TRL clarifies what technical proof investors expect next, while BRL ensures founders pursue the right capital (grants, Seed, Series A, partnerships) rather than prematurely raising institutional money without commercial credibility.
- **They reduce execution risk tied to founder inexperience.**
  First-time biotech founders are more likely to underestimate timelines, CMC (chemistry, manufacturing, and controls) complexity, and regulatory friction. TRL forces discipline around development sequencing, while BRL highlights execution gaps – e.g., governance, CRO (contract research organization) oversight, reimbursement logic – that commonly derail inexperienced teams.
- **They explain valuation inflection points objectively.**
  Valuation step-ups in biotech correlate more strongly with clinical, regulatory and pre-commercial/commercial milestone progression - which TRL and BRL help quantity rather than with company age or branding. Frameworks like TRL/BRL help first-time founders credibly justify valuation changes at Phase I entry, Breakthrough designation, or Phase II efficacy, rather than relying solely on narrative or anecdotal information.
- **They increase credibility with partners and regulators.**
  Strategic partners, pharma BD teams, and regulators implicitly assess both readiness dimensions. First-time founders who can clearly articulate their TRL and BRL status signal maturity, self-awareness, and reduced partnership risk - qualities that materially improve future funding diligence outcomes.

For first-time biotech founders, TRL and BRL provide a shared language for de-risking science, aligning capital to milestones, and translating clinical progress into credible progress towards commercial readiness.

Please review the table below for a clearer understanding of the logical progression and trade-offs of a biotech venture's entrepreneurial journey.

- **Vertical: TRL** *(Scientific / Clinical Readiness)*
- **Horizontal: BRL** *(Business / Commercial Readiness)*

NOTE: The effectiveness of an ESO depends on the match between the organization's expertise, focus, and stage of the startup. A poorly matched ESO may not accelerate readiness effectively.

Matching Your Venture with Right Fit ESO

	Low BRL (Early / Fragile Business Readiness)	High BRL (Credible / Investable Readiness)
Low TRL (Discovery / Early Preclinical)	**FOUNDATION & TRANSLATION ZONE** • Venture formation and team scaffolding • IP strategy, freedom-to-operate framing, and licensing readiness • Translation of discovery science into a coherent venture narrative • Non-dilutive capital strategy (SBIR/STTR, translational grants) • Early regulatory and milestone mapping *ESO role: Support in converting scientific promise into a fundable, structured venture without forcing premature commercialization.*	**DISCIPLINED ALIGNMENT ZONE** • Ensures business ambition remains grounded in scientific validation • Aligns capital strategy with realistic development milestones • Helps founders pace commercialization activities appropriately • Protects credibility with investors by avoiding overreach *ESO role: Support in maintaining alignment between science, milestones, and capital—preventing value erosion before technical inflection points.*
High TRL (Preclinical → Clinical Entry)	**READINESS ACCELERATION ZONE** • Accelerates business and operational readiness • Regulatory, CMC, and clinical execution planning • Investor diligence preparation and governance discipline • Board, advisory, and CRO infrastructure support *ESO role: Support in closing the execution gap so strong science translates into investable, partnerable readiness.*	**SCALE & STRATEGIC OPTIONS ZONE** • Targeted acceleration and strategic refinement • Partnering, licensing, and exit preparation • Signal amplification with investors and pharma • Ecosystem leverage without operational drag *ESO role: Providing optional but differentiated support that enhances outcomes without impeding investor or partner leadership.*

The right ESO can support advancing BRL across all stages - protecting value early, accelerating readiness midstream, and enhancing strategic outcomes at later stages.

Why Early Stage Biotech Ventures Seek Out Biotech Incubators

1

To translate strong science into investable milestones
The right incubator can provide support in converting discovery and preclinical progress into clear regulatory, clinical, and commercial proof points that investors and partners recognize and fund.

2

To accelerate business readiness without increasing scientific risk
Biotech incubators primarily advance business readiness (regulatory strategy, governance, capital planning, and execution discipline) while allowing scientific teams to stay focused on R&D.

3

To design a realistic regulatory and capital pathway early
Early support helps founders align IND planning, CMC considerations, and funding strategy - reducing costly missteps and premature fundraising.

4

To improve credibility with investors and pharma partners
Association with a reputable incubator can signal execution experience, disciplined planning, and reduced team risk - factors that materially influence diligence outcomes with early investors and non-dilutive grant programs (primarily SBIR/STTR).

5

To preserve control and valuation in early rounds
By strengthening milestones, data/AI strategy, and capital timing, the right incubators can help companies raise the right capital at the right time, avoiding reactive financing and onerous investment outcomes.

Figure 1: Sample TRL and BRL ranges for Drug Development Startups

NOTE: TRL ranges reflect adaptation from NASA/NHLBI frameworks to drug development. BRL ranges are the authors' indicative assessment; no standardized BRL scale exists for therapeutics.

Development Stage	TRL Range	BRL Range	Rationale
Discovery	1-2	1-2	Basic scientific principles observed; hypothesis formation; no validated product or commercial model. Commercial activity limited to early IP strategy and academic validation.
Preclinical	3-4	2-3	Proof-of-concept demonstrated in vitro/in vivo; IND-enabling underway. Business model forming, early market segmentation, seed financing, and translational grants.
Breakthrough Designation	5-6	3-4	*TRL: Typical designation in late phase 1 or early phase 2* *BRL: where valuation inflection begins but commercialization risk remains*
Clinical Entry (Phase I)	5-6	3-4	First-in-human validation of safety and PK/PD. Asset risk materially reduced. Business readiness includes Series A, CRO infrastructure, and regulatory engagement.
Clinical Expansion (Phase II)	6-7	4-5	Demonstrated clinical efficacy signal and defined regulatory pathway. Commercial strategy, payer logic, and partnering discussions actively underway.
Phase III Completed / Commercialization	8-9	5-6	Pivotal trials completed; regulatory approval; manufacturing and scale-up validated. Full commercial execution, reimbursement, distribution, and lifecycle strategy.

TRL Takeaway

TRL reflects scientific and clinical de-risking. In therapeutics, meaningful TRL advancement occurs at defined inflection points - proof of concept, first-in-human safety, and demonstrated clinical efficacy - while regulatory designations signal promise but do not substitute for clinical evidence.

BRL Takeaway

BRL captures economic and execution readiness. Regulatory incentives, such as Breakthrough Therapy and Orphan Drug Designation, can accelerate BRL ahead of TRL by enhancing capital efficiency, improving regulatory predictability, and refining reimbursement assumptions, even while clinical and commercialization risks persist.

Putting it All Together: Some Fictitious Biotech Startups for Determining TRL and BRL

Consider the key startup characteristics and relate them to the corresponding development stage in the matrix above. It becomes clearer how specific business model characteristics and milestones can influence a biotech startup to have a lower BRL than TRL.

Figure 2: Fictitious Biotech Startups for Determining TRL and BRL (Framework for the application of previous page learnings)

Startup	Therapeutic Area	Development Stage	TRL	BRL	Regulatory Designations	Salient Startup Characteristics
NeuroVanta Therapeutics	Neuro-degeneration (ALS / FTD)	Discovery → Early Preclinical	3	2	None	• Novel ASO mechanism targeting RNA splicing • In vitro + early in vivo target validation • University-licensed provisional IP • SBIR Phase I funded; no IND plan yet
OncoNext Therapeutics	Precision Oncology	Clinical Entry (Phase I)	5–6	3–4	Breakthrough Therapy Designation	• First-in-class small-molecule inhibitor • Strong early safety + efficacy signal • Breakthrough designation supports accelerated pathway • Series A raised; CRO-led clinical ops
Immunova Therapeutics	Autoimmune / Inflammatory Disease	Clinical Expansion (Phase II complete)	7–8	5	None	• Monoclonal antibody with Phase II efficacy • FDA-aligned pivotal trial design • Scalable CMC[1] validated • HEOR and payer logic established
Lysogenyx Therapeutics	Ultra-Rare Pediatric Disease	Phase I/II (Orphan Pathway)	5–6	4	Orphan Drug Designation	• Enzyme replacement therapy for <1,000 patients globally • Natural history data de-risks development • Orphan exclusivity + tax credits improve economics (currently 25% of qualified clinical testing under US law) • Higher pricing leverage; smaller trials

[1] *CMC is how you prove your drug can be made reliably, safely, and at scale - not just that it works.*

The right incubators and accelerators primarily help advance BRL, not TRL - helping founders translate scientific progress into credible, fundable, and partnerable ventures well before clinical inflection points.

Designation Stacking: Beyond Breakthrough Therapy or Orphan Drug designations, when relevant, some biotech companies pursue multiple FDA designations concurrently, to layer regulatory incentives, potentially creating a more efficient path forward.

Founder Takeaways: Funding & Readiness in Therapeutics

Therapeutics startups operate in a uniquely long, capital-intensive, and high-risk environment. Progress - and funding - are unlocked through disciplined de-risking, and milestone management not speed.

- **Acknowledge the risk reality.** Drug development timelines typically span 10-15 years, success rates are low, and capital requirements are substantial. Alignment between ambition and risk tolerance is essential.
- **Be precise about readiness.** Scientific progress (**TRL**) and business readiness (**BRL**) advance at different speeds, and misalignment between them often leads to stalled funding, false starts, and valuation friction. An objective, factual evaluation of your venture's successes and failures - *its proof points* - is just as important as reporting progress.
- **Design milestones around proof, not promise.** Capital follows clear inflection points – IND clearance, first-in-human data, and demonstrated clinical efficacy - not a venture's narrative alone.
- **Plan funding around regulatory logic.** Funding stages do not map cleanly to development phases; realistic milestone planning preserves credibility and control.
- **Build toward a likely exit.**

Clarity on risk, readiness, and milestones turns scientific progress into investable progress.

Abbreviations

ID: Target identification

SAB: Scientific Advisory Board

TPP: Target Product Profile

Pre-IND: Investigational New Drug

PK/PD: Pharmacokinetics (PK) and Pharmacodynamics (PD) studies

NDA (New Drug Application): Used for chemically synthesized, small-molecule drugs (e.g., tablets, capsules).

BLA (Biologics License Application): Used for biological products derived from living organisms (e.g., monoclonal antibodies, vaccines, gene therapies).

KOL: Key Opinion Leader

BARDA: Biomedical Advanced Research and Development Authority

AI: Artificial Intelligence

FTO: Freedom to Operate

ESO: Entrepreneurial Support Organization

ASO: An antisense oligonucleotide (ASO) is a short, synthetic strand of nucleic acid (typically 15–25 nucleotides) designed to bind to a specific RNA sequence

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