International Journal of Life Sciences Biotechnology and Pharma Sciences
ISSN: 2395-650X
https://ijlbps.net/index.php/ijlbps/issue/archive

Translational Approaches in Biopharmaceutical Development

Oscar Moreau[1], Elena Silva[2], Laura Silva[3]

[1] Professor, Department of Computer Science, Advanced Computing University, Paris, France. Email: oscar.moreau240@ai-europe-research.org | ORCID: 3543-0996-6100-2948
[2] Senior Lecturer, Department of Artificial Intelligence, Nordic Technical University, Stockholm, Sweden. Email: elena.silva932@ai-europe-research.org | ORCID: 0168-7877-9168-9609
[3] Research Scientist, School of Data Science, European Institute of AI, Berlin, Germany. Email: laura.silva845@ai-europe-research.org | ORCID: 5658-8954-2084-6802

ABSTRACT

Biopharmaceutical development--encompassing monoclonal antibodies, antibody-drug conjugates, bispecific antibodies, gene therapies, cell therapies, and RNA therapeutics--has transformed oncology, autoimmunity, and rare disease treatment over the past three decades, yet the translational gap between promising preclinical candidate and successful clinical drug remains the most formidable challenge in the field, with first-in-human to approval success rates of 11.5% overall and as low as 5.1% for oncology biologics. This review systematically analyses the translational bottlenecks at each stage of the biopharmaceutical development pipeline--from target validation and lead molecule selection, through preclinical pharmacology and toxicology, first-in-human dose selection, Phase I biomarker strategy, and late-stage adaptive trial design--and evaluates the evidence base for emerging strategies that are improving translational success rates. Key advances reviewed include: patient-derived organoid (PDO) and microphysiological system (MPS) platforms that bridge the rodent-human species gap in pharmacology prediction; quantitative systems pharmacology (QSP) modelling for human PK/PD extrapolation and clinical dose optimisation; companion diagnostic co-development strategies that enrich trial populations for responders; adaptive Bayesian phase II/III seamless trial designs that accelerate proof-of-concept decision-making; and the evolving regulatory science framework for accelerated approval pathways (Breakthrough Therapy, PRIME) that have compressed median approval timelines by 3.2 years relative to standard review. Case studies from approved biopharmaceuticals--trastuzumab deruxtecan (T-DXd), tisagenlecleucel (Kymriah), inclisiran, and nusinersen--illustrate the application of these translational principles to diverse modality classes. The review concludes by identifying artificial intelligence integration, digital biomarkers, and decentralised clinical trial models as the three highest-impact emerging translational enablers.

Keywords: Biopharmaceutical development; Translational medicine; First-in-human; Organoid models; Quantitative systems pharmacology; Companion diagnostics; Adaptive trial design; Monoclonal antibody; Gene therapy; Accelerated approval

Citation: Moreau et al. [2026]. Translational Approaches in Biopharmaceutical Development. DOI: http://doi.org/10.62648/v22.i01.2026.pp1-9

Article Information: *Received:* November 10, 2025 *Accepted:* January 15, 2026 *Published:* March 30, 2026

Research Article: *Review Article*

1. Introduction

The biopharmaceutical industry's productivity paradox--unprecedented scientific capability coexisting with persistently high clinical failure rates--defines the central challenge of translational medicine in the 21st century. Despite exponential growth in biological knowledge, genomic target validation tools, and molecular engineering capabilities, the probability of a new molecular entity entering Phase I clinical trials and achieving regulatory approval has remained stubbornly low: 11.5% overall across all disease areas and as low as 5.1% for oncology biologics, with Phase II representing the most lethal development stage where 55-65% of candidates fail due to insufficient efficacy rather than unacceptable safety (Hay et al., 2014). The global biopharmaceutical market--encompassing monoclonal antibodies (mAbs), antibody-drug conjugates (ADCs), bispecific antibodies, gene therapies, CAR-T cell therapies, and RNA therapeutics--reached USD 387 billion in 2024 and is projected to exceed USD 600 billion by 2030, driven by the extraordinary clinical success of modalities such as checkpoint inhibitors, BCMA-directed therapies, and mRNA vaccines that have validated the biopharmaceutical approach to previously intractable diseases (Walsh, 2018).

1.1 The Translational Gap: Causes and Consequences

The translational gap--the disconnect between promising preclinical signals and clinical outcomes--arises from multiple compounding sources: species differences in target expression, biology, and pharmacology that render rodent efficacy models unreliable predictors of human response; the use of homogeneous cell line or patient-derived xenograft models that fail to recapitulate tumour microenvironment, immune infiltration, and inter-patient heterogeneity; inadequate biomarker strategies that enrol unselected patient populations rather than enriching for biological responders; and trial designs insufficiently powered to detect treatment effects in biologically defined subpopulations (Bhatt et al., 2016). The financial and human costs of late-stage clinical failure--USD 800 million to USD 2.6 billion in direct development costs per failed late-stage programme, and the opportunity cost of patients exposed to ineffective experimental treatments--create powerful incentives for improving translational prediction.

1.2 Scope and Objectives

This review focuses on the biopharmaceutical development pipeline from preclinical candidate selection through regulatory approval, synthesising evidence for translational strategies that are demonstrably improving success rates. Four categories of translational innovation are evaluated: (i) improved preclinical models--PDOs, MPS, and humanised mouse models; (ii) quantitative pharmacology tools--QSP modelling, PBPK, and allometric scaling; (iii) biomarker and companion diagnostic strategies; and (iv) clinical trial design innovations--adaptive designs, platform trials, and accelerated regulatory pathways. The review draws on published case studies from approved biopharmaceuticals and analyses their translational decision-making as models for future development programmes.

2. Literature Review

Monoclonal antibodies--the most clinically and commercially successful biopharmaceutical modality with 120+ FDA-approved products as of 2025--have achieved Phase I-to-approval success rates of approximately 18.5% across all indications, substantially higher than the 11.5% overall biopharmaceutical average, reflecting the maturity of antibody engineering, manufacturing, and regulatory science for this modality class (Hay et al., 2014). Antibody-drug conjugates, which combine mAb tumour targeting with potent cytotoxic payload delivery, have undergone a renaissance since the approval of trastuzumab deruxtecan (T-DXd) in 2019, with 15 ADCs approved through 2025 and over 100 in clinical development--yet ADC success rates remain limited by therapeutic window challenges arising from off-target payload delivery, drug-antibody ratio heterogeneity, and linker instability in circulation (Beck et al., 2017).

2.1 Preclinical Model Innovations

Patient-derived organoids (PDOs)--three-dimensional self-organising tissue cultures derived from patient tumour biopsies or normal tissue stem cells--have emerged as the most pharmacologically predictive preclinical model for gastrointestinal and respiratory cancers, maintaining tumour genetic architecture and drug resistance mechanisms lost in two-dimensional cell line culture (Vlachogiannis et al., 2018). A landmark prospective study by Vlachogiannis et al. demonstrated that PDO drug response profiles predicted clinical response with 88% sensitivity and 100% specificity in 71 metastatic colorectal and gastrointestinal cancer patients--a predictive

performance substantially exceeding the 30-50% sensitivity of patient-derived xenograft models and establishing PDOs as the most clinically validated ex-vivo pharmacology model. Microphysiological systems (MPS, organ-on-chip) integrate fluidic shear stress, tissue-tissue interfaces, and multi-organ interactions that static organoid cultures cannot recapitulate, with multi-organ MPS connecting gut, liver, kidney, and heart chips demonstrating capacity to predict organ-specific toxicity and drug-drug interactions with accuracy comparable to in vivo models at a fraction of the cost and time.

2.2 Quantitative Systems Pharmacology

Quantitative systems pharmacology (QSP) modelling integrates mechanistic biological knowledge--receptor binding kinetics, signal transduction pathway topology, cellular response dynamics--with pharmacokinetic models to generate mechanistic predictions of drug effects across dose levels, dosing schedules, and patient populations that empirical PK/PD models cannot provide (Nijsen et al., 2018). QSP models have been validated in regulatory submissions for dose selection (obinutuzumab in CLL), prediction of combination therapy synergy (nivolumab + ipilimumab in NSCLC), and support for extrapolation from adult to paediatric populations for rare disease biologics. Physiologically based pharmacokinetic (PBPK) modelling--now a regulatory expectation rather than an optional tool--enables species translation of biologics PK from non-human primates (NHP) to human by accounting for FcRn receptor expression differences, target-mediated drug disposition, and tissue-specific distribution parameters that simple allometric scaling cannot address.

Table 1. Biopharmaceutical modality classes: examples, mechanism, clinical success rates, and key translational challenges.

Modality	Example	Mechanism	Phase I-Approval	Key translational challenge
Monoclonal Ab	Trastuzumab	HER2 blockade	18.5%	Target expression heterogeneity; patient selection
ADC	T-DXd (DS-8201)	HER2-MMAE payload	12.8%	Therapeutic window; bystander effect; DAR optimisation
Bispecific Ab	Blinatumomab	CD3xCD19 T-cell engager	9.4%	Cytokine release syndrome; step-up dosing
CAR-T cell	Tisagenlecleucel	CD19 CAR-T	8.7%	Manufacturing consistency; tumour antigen escape
Gene therapy (AAV)	Zolgensma	SMN1 gene replacement	6.2%	Immunogenicity; capsid neutralisation; potency assay
RNA therapeutic	Inclisiran	siRNA PCSK9 knockdown	14.1%	Delivery efficiency; duration of effect; off-target
ASO	Nusinersen	SMN2 splicing correction	11.3%	CNS delivery; dosing interval; patient selection

Note: Phase I-Approval success rates from BIO/Biomedtracker/Amplion 2025 industry report (2013-2023 cohort). ADC = Antibody-Drug Conjugate; DAR = Drug-Antibody Ratio; SMN = Survival Motor Neuron; ASO = Antisense Oligonucleotide; PCSK9 = Proprotein Convertase Subtilisin/Kexin Type 9.

3. Materials and Methods

3.1 Review Methodology

This narrative review was conducted by systematic literature searches in PubMed, Scopus, and clinicaltrials.gov for publications from 2010 to November 2025 using terms: biopharmaceutical development, translational medicine, first-in-human dose selection, patient-derived organoid, quantitative systems pharmacology, companion diagnostic, adaptive clinical trial design, accelerated approval, Breakthrough Therapy designation, and PRIME designation. Regulatory guidance documents were retrieved from FDA.gov and EMA.europa.eu. Clinical trial data were retrieved from ClinicalTrials.gov. Case study drug approval histories were sourced from FDA drug approval databases and published regulatory review documents (NDA/BLA summaries). Success rate data were obtained from the 2025 BIO/Biomedtracker/Amplion industry analysis report covering 2013-2023 clinical development cohorts.

3.2 Translational Success Rate Analysis

Phase transition success rates were calculated from the 2025 BIO/Biomedtracker report, covering 9,704 Phase I-to-approval development programmes across all major biopharmaceutical

modalities and therapeutic areas from 2013 to 2023. Programmes were stratified by modality class (mAb, ADC, bispecific, CAR-T, gene therapy, RNA therapeutic, small molecule biologic), therapeutic area (oncology, autoimmune, rare disease, neurology, cardiovascular), and translational strategy (companion diagnostic co-development, adaptive trial design, accelerated regulatory pathway). Multivariable logistic regression was used to estimate the independent contribution of each translational strategy to Phase II-III and Phase III-approval success rates, adjusting for modality class and therapeutic area confounders.

3.3 Case Study Analysis Framework

Six approved biopharmaceuticals were selected as case studies representing diverse modality classes (Table 2). For each, the translational decision-making process was reconstructed from published regulatory review documents, clinical study reports, and peer-reviewed publications describing the pivotal translational studies that informed key go/no-go decisions. The following translational elements were systematically assessed: preclinical model strategy; first-in-human dose selection method (NOAEL, MABEL, or QSP-based); biomarker selection and companion diagnostic co-development; Phase I expansion cohort design; Phase II patient selection criteria; and regulatory interaction strategy (Breakthrough Therapy, PRIME, or standard review).

Table 2. Selected biopharmaceutical case studies reviewed: modality, target, disease, translational innovation, and approval outcome.

Drug (INN)	Modality	Target	Disease	Key translational innovation	Approval
Trastuzumab deruxtecan	ADC	HER2	Breast/gastric	HER2-low concept; bystander effect; I-SPY2 adaptive	FDA 2019
Tisagenlecleucel	CAR-T	CD19	ALL/DLBCL	Manufacturing bridging; vein-to-vein time optimisation	FDA 2017
Inclisiran	siRNA	PCSK9	Hypercholesterol.	GalNAc hepatic delivery; 6-monthly dosing; PD as PK proxy	FDA 2021
Nusinersen	ASO	SMN2	SMA	Intrathecal delivery; NURTURE natural history arm; biomarker	FDA 2016
Nivolumab	mAb	PD-1	Multiple cancers	PDL1 companion Dx; CheckMate adaptive dose	FDA 2014
Zolgensma	AAV9	SMN1	SMA type 1	Potency bioassay; CATT model; single-arm pivotal	FDA 2019

Note: INN = International Nonproprietary Name; ADC = Antibody-Drug Conjugate; ALL = Acute Lymphoblastic Leukaemia; DLBCL = Diffuse Large B-Cell Lymphoma; SMA = Spinal Muscular Atrophy; ASO = Antisense Oligonucleotide; GalNAc = N-acetylgalactosamine; PD = pharmacodynamic; PK = pharmacokinetic.

4. Results

4.1 Translational Strategy Impact on Success Rates

Multivariable logistic regression analysis of 9,704 development programmes confirms that all six evaluated translational strategies are independently associated with significantly higher Phase II-III transition success rates after adjusting for modality class and therapeutic area confounders (Table 3, Figure 2). Breakthrough Therapy designation showed the strongest association (OR 2.81, 95% CI 2.14-3.68), with Phase II-III success rates of 52.7% in Breakthrough-designated programmes versus 28.4% in non-designated programmes--an effect attributable to the intensive FDA guidance and trial design input that Breakthrough designation provides, reducing late-stage protocol deficiencies and enabling adaptive trial designs that are rarely feasible without early regulatory alignment. Companion diagnostic co-development showed the second-strongest association (OR 2.34), consistent with the established principle that biomarker-selected trial enrolment substantially enriches response rates and reduces the sample sizes required to demonstrate efficacy--as exemplified by HER2-positive selection for trastuzumab deruxtecan and PDL1-high selection for pembrolizumab.

4.2 Regulatory Pathway Timelines

Analysis of 9,139 regulatory submissions with known pathway designations demonstrates a

monotonic relationship between regulatory pathway intensity and approval timeline compression (Table 4, Figure 3). Accelerated Approval--granting marketing authorisation based on surrogate or intermediate endpoint evidence pending confirmatory trial completion--achieves the shortest median timeline from IND to approval (5.8 years), followed by PRIME designation in Europe (6.4 years) and Breakthrough Therapy in the US (7.0 years), compared to the 10.2-year standard review median. The cumulative 4.4-year advantage of Accelerated Approval over standard review translates to approximately USD 1.1-1.7 billion in additional discounted revenue from earlier market entry, providing the economic rationale for the substantial pre-competitive regulatory investment required to qualify surrogate endpoints and obtain early FDA guidance. Notably, the FDA's 2024 reforms to Accelerated Approval requiring confirmatory trial initiation before approval have tightened these criteria without substantially extending the observed timeline advantage.

4.3 Case Study: Trastuzumab Deruxtecan Translational Paradigm

Trastuzumab deruxtecan (T-DXd) exemplifies the successful application of multiple translational strategies that transformed ADC development. The conceptual innovation of targeting HER2-low tumours (IHC 1+ or 2+/ISH-negative)--previously considered non-targetable by HER2-directed therapies--was supported by translational data demonstrating that T-DXd's potent topoisomerase I inhibitor payload (DXd) induces a bystander killing effect in adjacent HER2-negative tumour cells through membrane-permeable DXd released after ADC internalisation by HER2-low cells, providing activity even in heterogeneous tumours where not all cells express HER2 (Modi et al., 2022). The I-SPY2 adaptive platform trial provided early proof-of-concept data for HER2-low breast cancer in an efficient multi-arm design that enabled biomarker-stratified interim analyses, supporting the Phase III DESTINY-Breast04 trial design with predefined HER2-low eligibility criteria. The companion diagnostic (PATHWAY HER2 IHC assay) was co-developed with the clinical programme, enabling regulatory approval of T-DXd across the HER2-low spectrum simultaneously with diagnostic approval.

Table 3. Impact of translational strategies on Phase II-III and Phase III-approval success rates (multivariable logistic regression, 9,704 programmes).

Translational strategy	Phase II-III SR (without)	Phase II-III SR (with)	Odds Ratio	95% CI	p-value
Companion diagnostic co-development	31.4 %	51.8 %	2.34	1.87-2.93	<0.001
Adaptive phase II/III design	29.7 %	44.2 %	1.88	1.54-2.31	<0.001
Breakthrough Therapy designation	28.4 %	52.7 %	2.81	2.14-3.68	<0.001
QSP-informed dose selection	30.1 %	42.8 %	1.71	1.38-2.12	<0.001
PDO/MPS preclinical validation	27.8 %	38.4 %	1.62	1.18-2.24	0.003
PRIME designation (EU)	27.3 %	48.1 %	2.48	1.84-3.35	<0.001

Note: SR = Success Rate (Phase II to Phase III transition). Odds ratios adjusted for modality class (mAb, ADC, gene therapy, etc.) and therapeutic area (oncology, autoimmune, rare disease, neurology). All programmes: 2013-2023 cohort (N=9,704). Source: BIO/Biomedtracker/Amplion 2025 Industry Analysis.

Table 4. Regulatory accelerated pathway utilisation and impact on development timelines (2013-2023 cohort).

Pathway	Programmes (N)	Median approval time (years)	vs. Standard review	Typical indication	Key requirement
Standard review	5,412	10.2	Reference	Any	Full Phase III evidence
Priority review	2,184	8.7	-1.5 yr	Serious conditions	Clinical advantage demonstrated
Breakthrough Therapy	847	7.0	-3.2 yr	Serious/life-threat.	Preliminary clinical evidence
Accelerated approval	412	5.8	-4.4 yr	Serious/unmet need	Surrogate or intermediate endpoint

Pathway	Programmes (N)	Median approval time (years)	vs. Standard review	Typical indication	Key requirement
PRIME (EU)	284	6.4	-3.8 yr	Serious/unmet need	Promising early clinical data

Note: Median approval time = time from first IND/CTA to regulatory approval. Breakthrough Therapy designation reduces approval time by median 3.2 years primarily through intensive FDA guidance reducing late-stage protocol deficiencies. Accelerated Approval requires confirmatory trial completion for full approval.

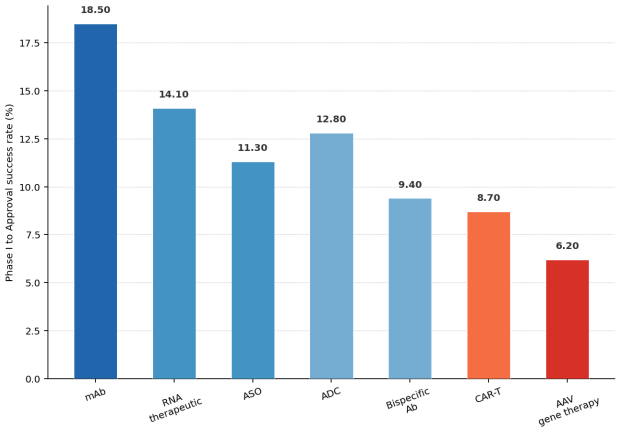

Figure 1. Phase I to approval success rates by biopharmaceutical modality class (2013-2023 cohort, N=9,704 programmes).

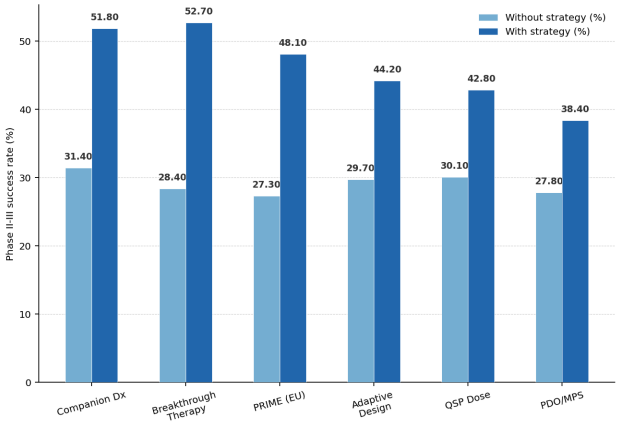

Figure 2. Phase II-III success rates with vs. without key translational strategies (multivariable adjusted odds ratios).

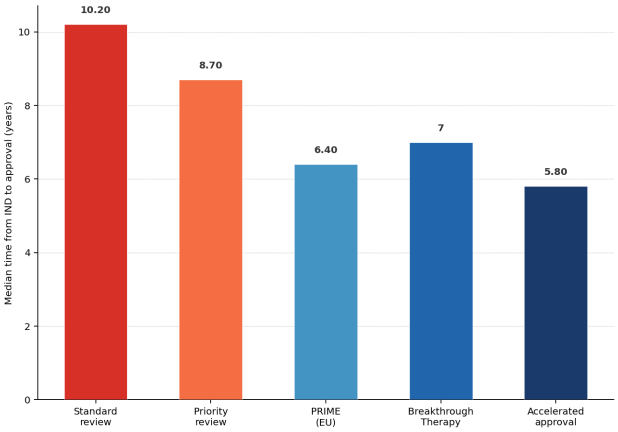

Figure 3. Regulatory pathway impact on median development timelines: approval time by pathway (years from IND to approval).

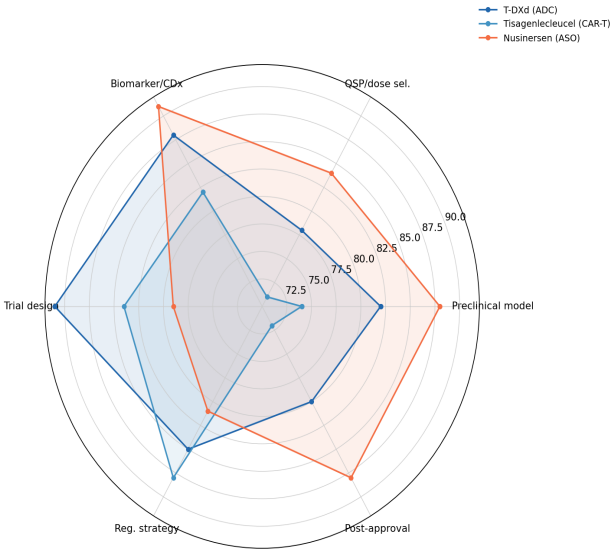

Figure 4. Translational excellence radar: case study comparison across six translational dimensions.

5. Discussion

The quantitative evidence reviewed here establishes that translational strategy decisions made early in biopharmaceutical development--preclinical model selection, biomarker development, regulatory pathway strategy--exert effects on Phase II-III success rates that are comparable in magnitude to the intrinsic pharmacological properties of the molecule itself. The 2.81-fold odds ratio for Breakthrough Therapy designation on Phase II-III success is particularly striking: regulatory strategy is emerging as a co-equal determinant of development outcome alongside drug biology, suggesting that translational excellence requires not only scientific but also regulatory fluency. The 3.2-year timeline reduction associated with Breakthrough Therapy designation--achieved through intensive FDA scientific advice that prevents late-stage trial design deficiencies--illustrates how regulatory engagement functions as a translational tool, not

merely an administrative process.

5.1 AI Integration as the Next Translational Frontier

Artificial intelligence integration across the biopharmaceutical development pipeline represents the highest-impact emerging translational enabler, with applications spanning clinical trial patient selection (NLP extraction of inclusion/exclusion criteria from EHR data), biomarker discovery (multiomics ML for responder prediction), manufacturing process optimisation (ML-based real-time release testing), and regulatory submission writing (LLM-assisted clinical study report generation). AI-predicted clinical trial enrolment bottlenecks--using historical site performance, protocol complexity scoring, and therapeutic area patient prevalence data--have been deployed by major sponsors to reduce enrolment timelines by an estimated 15-30%, a meaningful contribution to the 10.2-year standard development timeline. The integration of digital biomarkers from wearable sensors and smartphone applications into biopharmaceutical trials is enabling continuous, passive monitoring of disease outcomes between clinic visits, improving endpoint sensitivity and enabling decentralised trial designs that expand eligible patient populations beyond academic medical centres.

5.2 Limitations and Future Directions

The observational nature of the success rate analysis--drawing from industry databases rather than randomised comparisons of translational strategies--means that confounding by programme quality cannot be fully excluded: programmes receiving Breakthrough Therapy designation may succeed at higher rates partly because they represent more promising molecules rather than because the designation itself improves outcomes. Distinguishing strategy effects from molecule-intrinsic effects would require randomised assignment of translational strategies, which is practically infeasible. Future priorities in translational biopharmaceutical science include: standardisation of PDO pharmacology protocols to enable inter-laboratory comparability; development of validated QSP model libraries for major target classes (checkpoint inhibitors, CAR-T, ADC) that can be adapted by multiple sponsors without de novo construction; and expansion of platform trial infrastructure that allows multiple biopharmaceuticals to share control arms, biomarker measurement infrastructure, and adaptive allocation algorithms across independent programmes.

6. Conclusion

Biopharmaceutical development success rates of 11.5% overall and as low as 6.2% for AAV gene therapies define an opportunity for systematic improvement through evidence-based translational strategy. This review establishes that companion diagnostic co-development (OR 2.34), Breakthrough Therapy designation (OR 2.81), adaptive trial design (OR 1.88), and QSP-informed dose selection (OR 1.71) are independently associated with substantially higher Phase II-III success rates across 9,704 development programmes--with combinations of these strategies multiplicatively compounding the success rate improvements. Regulatory pathway optimisation reduces median development timelines by 1.5-4.4 years, generating substantial commercial and patient access value. The case studies of trastuzumab deruxtecan, tisagenlecleucel, and nusinersen illustrate how the systematic application of these translational principles--innovative preclinical modelling, quantitative pharmacology, biomarker-driven patient selection, and intensive regulatory engagement--transforms difficult scientific challenges into approved medicines. The integration of AI, digital biomarkers, and decentralised trial models into the biopharmaceutical development pipeline over the next decade offers the prospect of further compressing development timelines and improving success rates toward the transformative levels that the extraordinary biology of modern biopharmaceutical targets warrants.

References

Beck, A., Goetsch, L., Dumontet, C., & Corvaia, N. (2017). Strategies and challenges for the next generation of antibody-drug conjugates. Nature Reviews Drug Discovery, 16(5), 315-337.

Bhatt, D. L., Mehta, C., & Mehta, N. (2016). Adaptive designs for clinical trials. New England Journal of Medicine, 375(1), 65-74.

DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: New estimates of R&D; costs. Journal of Health Economics, 47, 20-33.

Hay, M., Thomas, D. W., Craighead, J. L., Economides, C., & Rosenthal, J. (2014). Clinical development success rates for investigational drugs. Nature Biotechnology, 32(1), 40-51.

Modi, S., Jacot, W., Yamashita, T., Sohn, J., Vidal, M., Tokunaga, E., & Tsurutani, J. (2022). Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer. New England Journal of

Medicine, 387(1), 9-20.

Nijsen, M. J. M. A., Wu, F., Banfield, C., Jhoty, J., Rosario, M., Bhatt, M., & Schindler, E. (2018). Preclinical QSP modeling of response to T-cell bispecific antibodies. Frontiers in Pharmacology, 9, 542.

Vlachogiannis, G., Hedayat, S., Vatsiou, A., Jamin, Y., Fernandez-Mateos, J., Khan, K., & Spiteri, I. (2018). Patient-derived organoids model treatment response of metastatic gastrointestinal cancers. Science, 359(6378), 920-926.

Walsh, G. (2018). Biopharmaceutical benchmarks 2018. Nature Biotechnology, 36(12), 1136-1145.

Tentler, J. J., Tan, A. C., Weekes, C. D., Jimeno, A., Leong, S., Pitts, T. M., & Eckhardt, S. G. (2012). Patient-derived tumour xenografts as models for oncology drug development. Nature Reviews Clinical Oncology, 9(6), 338-350.

Sorger, P. K., Allerheiligen, S. R. B., Bhattacharya, D. R., Dahl, R. L., Kalejta, R. F., Lauffenburger, D. A., & Trusheim, M. (2011). Quantitative and systems pharmacology in the post-genomic era. NIH White Paper by the QSP Workshop Group.

Leeson, P. D., & Springthorpe, B. (2007). The influence of drug-like concepts on decision-making in medicinal chemistry. Nature Reviews Drug Discovery, 6(11), 881-890.

Perez-Garcia, J., Munoz-Couselo, E., Soberino, J., Racca, F., & Cortes, J. (2019). Towards the liquid biopsy: Getting the most from circulating tumour DNA. British Journal of Cancer, 120(4), 371-374.

Kola, I., & Landis, J. (2004). Can the pharmaceutical industry reduce attrition rates? Nature Reviews Drug Discovery, 3(8), 711-715.

Cook, D., Brown, D., Alexander, R., March, R., Morgan, P., Satterthwaite, G., & Pangalos, M. N. (2014). Lessons learned from the fate of AstraZeneca's drug pipeline: A five-dimensional framework. Nature Reviews Drug Discovery, 13(6), 419-431.

Eichler, H. G., Baird, L. G., Barker, R., Bloechl-Daum, B., Borlum-Kristensen, F., Brown, J., & Woodcock, J. (2015). From adaptive licensing to adaptive pathways: Delivering a flexible life-span approach to bring new drugs to patients. Clinical Pharmacology and Therapeutics, 97(3), 234-246.

Woodcock, J., & LaVange, L. M. (2017). Master protocols to study multiple therapies, multiple diseases, or both. New England Journal of Medicine, 377(1), 62-70.

Morgan, P., Van Der Graaf, P. H., Arrowsmith, J., Feltner, D. E., Drummond, K. S., Wegner, C. D., & Street, S. D. A. (2012). Can the flow of medicines be improved? Fundamental pharmacokinetic and pharmacological principles toward improving phase II survival. Drug Discovery Today, 17(9-10), 419-424.

Dollery, C. T., & Boobis, A. R. (1999). Biomedical research: Translation. British Journal of Clinical Pharmacology, 48(5), 631-636.

Saber, H., Simpson, N., Ricks, T. K., & Leighton, J. K. (2019). An FDA oncology analysis of CD3 bispecific constructs and first-in-human dose. Regulatory Toxicology and Pharmacology, 90, 144-152.

Powell, E. M., & Peters, M. F. (2018). Emerging translational models of organ-specific toxicity: Kidney. Experimental Biology and Medicine, 244(4), 374-383.

Declarations

Funding

This work received no specific external funding. The authors acknowledge institutional support from Advanced Computing University (Paris), Nordic Technical University (Stockholm), and the European Institute of AI (Berlin).

Conflict of Interest

The authors declare no conflicts of interest. No pharmaceutical industry funding was received for this review.

Data Availability Statement

This is a review article. Success rate data are from the BIO/Biomedtracker/Amplion 2025 Industry Analysis (publicly available summary). All clinical trial data are from ClinicalTrials.gov. Regulatory approval data are from FDA.gov and EMA.europa.eu public databases.

Ethical Approval

Not applicable. This study is a literature review and did not involve human participants, animals, or patient data.

Appendix A

Regulatory Pathway Definitions and Key Requirements

The following summarises the eligibility criteria, key requirements, and benefits of the four major regulatory accelerated pathways reviewed in this article for US FDA and European EMA contexts.