

An Operational Roadmap for Drug Repurposing of Registered Pharmaceuticals: A Four-Stage Model Bypassing Early Clinical Phases

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Research Article

Keywords: Drug repurposing, Phase IV clinical trial, Industrial property protection, Method-of-use patent, Regulatory strategy, Incremental innovation

Posted Date: August 31st, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10359497/v1>

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Additional Declarations: Competing interest reported. Aqui está o texto da declaração de competing interests com o ajuste de precisão aplicado: Financial interests: Heros Teixeira Rabelo is an employee of Laboratório Gross S.A., the marketing authorization holder of Organoneuro Cerebral® and the entity that funded the Phase IV clinical study described in this article. Laboratório Gross S.A. is the direct commercial beneficiary of the repurposing strategy reported here. This competing interest was declared to the Research Ethics Committee, which approved the study protocol, and the clinical results were peer-reviewed and published in an indexed journal. Wanise Borges Gouvea Barroso and Marcus Vinicius Nora de Souza declare they have no financial interests. Non-financial interests: none.

Abstract

Background

Developing a new active pharmaceutical ingredient exceeds one billion dollars over more than a decade, with failure rates above 90% — a prohibitive barrier for mid-sized manufacturers, whose registered portfolios remain therapeutically underexploited. Repurposing is a recognised response, yet the literature offers no replicable operational model covering the full sequence from candidate indication to regulatory approval and intellectual property protection.

Objectives

To present and operationalize a four-stage roadmap for obtaining a new therapeutic indication from an already registered drug (the parent product), and to define the conditions under which it is replicable by mid-sized manufacturers.

Methods

The model was constructed through retrospective and prospective analysis of a completed repurposing programme: the parent product, a GABA/B-vitamin formulation registered in Brazil since 1973, repurposed for motion sickness (spin-off). It comprises four sequential stages: (1) Scientific Basis; (2) Industrial Property Protection; (3) Validation via a Phase IV Clinical Study; and (4) Construction of the Regulatory Dossier from the Parent Product. Stage deliverables were derived from the executed programme and refined by explicit identification of a sequencing limitation encountered during it.

Results

The Phase IV trial ($n = 335$, single centre, ClinicalTrials.gov NCT05221892) showed superiority of the parent product over the active comparator on the primary Motion Sickness Assessment Questionnaire endpoint, reaching the conventional significance threshold ($p = 0.05$). The spin-off trademark was granted by the Brazilian patent office (INPI) in February 2026; the regulatory dossier was submitted to Anvisa in July 2023 (Process No. 25991.006003/77); a method-of-use patent was filed in June 2026. Direct entry into Phase IV eliminated preclinical studies and Phases I–III — approximately 65–75% of conventional development costs and eight to twelve years of timeline.

Conclusion

The model offers a replicable, cost-effective path to incremental innovation through repurposing. Positioning Industrial Property Protection as Stage 2 — before clinical investigation and any public

disclosure — maximizes patentable claim scope and the effective window of commercial exclusivity, a structural advantage specific to the repurposing pathway.

Trial registration:

ClinicalTrials.gov NCT05221892, registered 3 February 2022.

1. Introduction

The development of new active pharmaceutical ingredients requires massive investments, often exceeding one billion dollars over more than a decade, with clinical failure rates above 90% in all therapeutic areas [1, 2]. For small and medium-sized pharmaceutical companies, this financial barrier makes the search for new products with unique characteristics economically unfeasible. The result is a structural paradox: companies with mature product portfolios systematically underutilize the therapeutic potential embedded in them.

Drug repurposing has emerged as a strategic response to this paradox. Broadly defined as the clinical and regulatory validation of a new therapeutic indication for an already approved drug, repurposing has attracted increasing academic interest [3, 4]. The literature documents well-known cases of successful repurposing — sildenafil for erectile dysfunction, thalidomide for multiple myeloma, metformin for polycystic ovary syndrome. The theoretical advantages are consistently cited: cost reduction, accelerated timelines, and lower risk of clinical failure [3]. However, despite this theoretical recognition, the repurposing literature has not yet produced replicable operational models to guide a pharmaceutical company through the entire sequence — from the search for a new therapeutic indication to the protection of intellectual property and regulatory approval. The available frameworks are predominantly conceptual or descriptive [5, 6]; operational guidance for companies without large clinical development departments remains largely absent.

1.1 Drug repurposing: taxonomy and strategic context

We adopt the following operational definition: drug repurposing is the clinical validation and regulatory approval of a new therapeutic indication for a previously registered drug [5, 6]. The literature identifies three structurally distinct pathways [3]: serendipitous repositioning, computational repositioning, and repositioning induced by a regulatory trigger. The model proposed in this article is structurally applicable to all three; the illustrative programme belongs to the third.

The structural advantages of drug repurposing — an estimated 50–70% reduction in timelines and a 65–75% reduction in costs — arise because the product’s safety profile, pharmacokinetics, and CMC documentation are already accepted by the regulatory agency [3, 7]. The central argument of this article is that these advantages should be deliberately structured into a methodology that explicitly exploits the

existing regulatory asset at each stage, while protecting intellectual property from the earliest signal of therapeutic potential.

1.2 The phase bypass mechanism

In conventional pharmaceutical development, the preclinical stage and Phases I–III account for approximately 65–75% of total development costs and 8–12 years of the timeline [8, 9]. For a registered product, the scientific justification for these phases is substantially weakened: safety in humans is documented through post-marketing pharmacovigilance, the formulation is validated, manufacturing is certified, the CMC dossier is on file, and the pharmacokinetic profile is known.

A well-designed Phase IV study – randomized, blinded, controlled, with validated outcomes – can therefore provide the confirmatory evidence of efficacy and safety required for approval of the new indication. The Phase IV study fulfils the confirmatory role of Phase III in conventional development; the registered product’s safety history fulfils the role of Phases I and II.

1.3 Protection of industrial property in drug repurposing

The intellectual property dimension of drug repurposing is systematically underrepresented in the literature. Most existing frameworks focus on pharmacological and regulatory dimensions, treating intellectual property as a secondary consideration. The proposed model incorporates two complementary instruments – trademark registration and method-of-use patent filing – as a structural stage.

The commercial value of method-of-use patents in repurposing is substantial. Patents are granted for a nominal term of 20 years from filing [10]; in conventional development, the preclinical-to-Phase III timeline reduces effective exclusivity to 12–15 years [10, 11]. In the repurposing pathway, the Phase IV study is the only clinical investment required before regulatory submission, so the effective exclusivity window of a method-of-use patent is substantially closer to the 20-year nominal term – a structural advantage exclusive to the repurposing strategy and not previously documented in the literature.

Trademark protection offers indefinite protection through successive renewals, is universally available regardless of jurisdiction, and does not depend on novelty of composition or method. For jurisdictions where method-of-use patents are unavailable or unenforceable, trademark registration is the primary, universally applicable instrument for intellectual property protection.

1.4 Positioning in the literature and aim of the study

The model presented addresses the operational gap between the drug repurposing literature [3, 4] – which documents the pharmacological and regulatory dimensions without producing replicable frameworks for medium-sized manufacturers – and the incremental pharmaceutical innovation literature [5, 12] – which analyses portfolio extension strategies focusing on formulation or delivery system changes, not on approval of a new indication based on original clinical evidence.

The aim of this study is therefore to present and operationalize a four-stage roadmap for the repurposing of registered pharmaceuticals, to demonstrate its application through a completed real-world programme, and to define the preconditions under which it is replicable. The central structural element of the model is the phase bypass mechanism: the established safety profile, pharmacokinetic documentation, and CMC dossier of the registered product justify direct entry into Phase IV for the new indication, eliminating preclinical studies and Phases I–III. The model is jurisdiction-agnostic in Stages 1–3 and adapts to different regulatory frameworks in Stage 4.

2. Methods

2.1 Model construction

The model was developed from a real-world programme through combined retrospective and prospective analysis of the search for a new therapeutic indication for the parent product, a gamma-aminobutyric acid (GABA) formulation with B-complex vitamins registered and marketed in Brazil since 1973, for the new indication of motion sickness (spin-off marketed under the spin-off brand name). Each stage of the executed programme was analysed to extract its objective, methodological approach, key deliverables, and the specific structural advantage activated by the existing regulatory asset of the registered product. The model was subsequently refined when the authors identified that, with adjustments, the roadmap could be generalised beyond the originating programme to benefit other pharmaceutical manufacturers.

The resulting model organizes the drug repurposing process into four sequential and cumulative stages (Fig. 1): (1) Scientific Basis; (2) Industrial Property Protection; (3) Validation of the New Therapeutic Indication through a Phase IV Clinical Study; and (4) Construction of the Regulatory Dossier from the Parent Product. The model is jurisdiction-agnostic in Stages 1 to 3; Stage 4 adapts to the target country's regulatory framework.

2.2 Stage 1 – Scientific Basis

Objective

To systematically document the therapeutic potential of the active compounds of the registered product for the new candidate indication, producing sufficient scientific evidence to support the regulatory dossier and justify conducting a Phase IV study.

Approach

A scoping review conducted according to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines is the recommended instrument. Scoping reviews are preferred over full systematic reviews because the evidence base for established formulations is typically heterogeneous – composed of preclinical, mechanistic, and observational

studies — lacking the methodological homogeneity required for quantitative meta-analysis. The review maps the pathways of action by which each active compound may contribute to the target indication and stratifies the evidence with a standardized taxonomy, such as SORT (Strength of Recommendation Taxonomy).

Key deliverables

(1) Narrative synthesis of the evidence base stratified by compound and level of evidence; (2) identification of the indication with the most robust signal; (3) scientific rationale document for inclusion in the regulatory dossier; (4) gap analysis specifying the requirements for the Phase IV study.

Structural advantage enabled

Leverages existing pharmacological literature without new experimental investment; establishes the scientific justification for direct entry into Phase IV at Stage 3. This stage functions as the model's investment control mechanism (Fig. 2) — its output either confirms the rationale for investment in Stages 2 to 4 or identifies gaps to be addressed before proceeding.

2.3 Stage 2 — Industrial Property Protection

Objective

To establish intellectual property protection for the repurposed product.

Approach

Two complementary instruments are mobilized at this stage. Trademark registration for the new commercial identity is the primary and universally applicable instrument — required in all jurisdictions, regardless of patent legislation, and a prerequisite for regulatory submission in many regulatory frameworks that require the declaration of the trade name in the new indication dossier. A method-of-use patent filing is a jurisdiction-dependent complement that, where available, offers exclusivity for a specified period for the specific therapeutic use.

Critical sequencing insight

This stage should be completed before any public disclosure (Stage 3), with the filings registered. Registration of the clinical study constitutes public disclosure of the therapeutic hypothesis and may affect the patent's novelty in jurisdictions with absolute novelty requirements. Trademark registration processing times must be managed in parallel with the preparation of Stage 4 to ensure that trademark registration occurs before regulatory submission requires the declaration of the trade name — a critical path interdependency documented in the illustrative programme.

Key deliverables

(1) Trademark registration application filed for the new trade name; (2) method-of-use patent application filed (when applicable in the jurisdiction); (3) documented and registered pre-disclosure protection.

Structural advantage enabled

Filing before disclosure maximizes the scope of patentable claims and the effective window of commercial exclusivity; trademark registration establishes the spin-off product's trade name regardless of the regulatory timeline.

2.4 Stage 3 – Validation of the New Therapeutic Indication through a Phase IV Study

Objective

To generate Level A clinical evidence (randomized clinical trial with patient-oriented outcomes, according to SORT criteria) for the new indication, sufficient to meet the regulatory standards for therapeutic indication approval.

Approach

A randomized, blinded, controlled Phase IV clinical trial designed to directly address the evidence gap identified in Stage 1. A registered, active comparator is preferable when available, as it simultaneously meets ethical requirements and generates competitive positioning data. Outcomes must be validated instruments; the primary outcome must meet the evidence standards of the target jurisdiction.

Rationale for entering Phase IV: The registered product status, the evidence of therapeutic potential from Stage 1, and the existing safety profile collectively constitute the scientific and regulatory rationale for entering Phase IV without the preceding phases. Ethics committees and regulatory agencies accept this entry point when: (a) safety in humans is documented by post-marketing pharmacovigilance; (b) the dose range is established; and (c) the rationale for the mechanism of action for the new indication is scientifically substantiated. The Phase IV study serves the confirmatory role of Phase III in conventional development; the registered product safety history serves the roles of Phases I and II.

Key deliverables

(1) Randomized clinical trial published in an indexed peer-reviewed journal; (2) full clinical study report; (3) adverse event profile consistent with the established safety profile.

Structural advantage enabled

Elimination of Phases I, II, and III – corresponding to approximately 65–75% of the total costs of new drug development (USD 300–700 million, eight to twelve years [8, 9]).

2.5 Stage 4 — Construction of the Regulatory Dossier from the Parent Product

Objective

To compile and structure the complete regulatory package for approval of the new indication, incorporating the CMC documentation of the parent product, the Phase IV clinical study report, and the evidence of therapeutic potential produced in Stage 1.

Approach: The dossier leverages the existing regulatory file of the parent product — CMC documentation, pharmacovigilance reports, manufacturing certifications, and stability data already on file with the agency. The new indication petition complements this existing file; the agency evaluates only incremental evidence for the new indication. This principle — incremental evaluation rather than full re-evaluation — manifests in jurisdiction-specific mechanisms: clone registration (Brazil, RDC 954/2024, which replaced RDC 31/2014), well-established use application (EU, Directive 2001/83/EC, Article 10a), and Supplemental NDA (USA, 21 CFR 314.54). Core components include: (1) safety and efficacy report integrating evidence from Stages 1 and 3; (2) updated package insert with the new indication and dosage; (3) updated labelling for the new trade identity; (4) scientific justification document.

Key deliverables

(1) Complete regulatory package in the required format; (2) supporting technical documents; (3) formal petition to the competent health authority.

Structural advantage enabled

The CMC dossier, pharmacovigilance documentation, and manufacturing certifications already on file with the agency eliminate the pharmaceutical development investment that precedes Phase I in conventional development — a precondition that the model relies upon from Stage 1 onward, rather than a further saving generated at Stage 4; the economics of the phase bypass are fully localized in Stage 3.

3. Results

This section reports the application of the four-stage model to the parent product / spin-off repurposing programme and the verifiable deliverable produced at each stage.

3.1 Product and repurposing context

The parent product is a multicomponent oral formulation marketed in Brazil since the 1970s, combining a GABAergic agent (gamma-aminobutyric acid) with its precursor amino acid (glutamic acid), a calcium salt, and B-complex vitamins (B1, B6, and B12) in a coated tablet.

The target indication — motion sickness — represents an unmet clinical need: available options are limited to anticholinergics (scopolamine) and first-generation antihistamines (dimenhydrinate, diphenhydramine, promethazine), all associated with sedation, dry mouth, blurred vision, and impaired motor performance [13, 14]. No non-sedating oral option with proven efficacy was available. The trigger for the repurposing effort was regulatory: Anvisa's RDC 242/2018 required manufacturers of vitamin/mineral/amino-acid combinations to present well-established clinical evidence within 60 months, creating the structural pressure that initiated the process.

3.2 Stage 1: Scientific Basis

A scoping review according to the PRISMA-ScR guidelines was conducted in nine databases and institutional sources (PubMed/Medline, SciELO Brazil, Scopus, ResearchGate, Google Scholar, Web of Science, BDTD, WHO, and Anvisa), using 13 descriptors in Portuguese and English. A complementary search using an artificial intelligence platform (Elicit Systematic Review) was conducted, drawing from a collection of over 100 million publications. In total, 62 studies were included in the final synthesis.

Evidence of therapeutic potential was documented for each active compound: GABA acts through GABAergic inhibition of velocity storage mechanisms in the vestibular nuclei complex [15, 16]; glutamic acid (a GABA precursor) participates in vestibular excitation–inhibition balance; pyridoxine (B6) supports biosynthesis of serotonin and dopamine, neurotransmitters involved in the emetic reflex; thiamine (B1) and cyanocobalamin (B12) provide complementary neurochemical support. The evidence was classified as SORT Level B overall, with a Level A (randomized clinical trial) gap identified as the requirement for Stage 3.

3.3 Stage 2: Industrial Property Protection — sequencing execution and limitation

The spin-off trademark ([trademark application]) was filed on 24 February 2023 — before publication of the clinical study (October 2023). Notably, however, registration of the trial at ClinicalTrials.gov (NCT05221892, 3 February 2022) preceded the trademark filing by approximately twelve months. The trademark was therefore deposited after the trial had already entered the public domain through its registry record. Because trademark protection does not depend on novelty, this sequence did not invalidate the trademark, which was duly granted on 24 February 2026 (Industrial Property Journal no. 2877, valid until 24 February 2036). Strictly speaking, however, fully pre-disclosure sequencing would require the trademark filing to precede even the ClinicalTrials.gov registration — a refinement the model presented here adopts for future applications. The interdependence between trademark and regulatory submissions was operationally relevant: Anvisa's SOLICITA electronic system requires the trade name to be declared at the time of submission, requiring parallel management of the trademark registration process at INPI and the dossier preparation.

The method-of-use patent application (BR 10 2026 014606 4) was filed on 12 June 2026 — approximately 32 months after publication of the clinical study and 40 months after the

ClinicalTrials.gov registration. Unlike trademark protection, patent novelty is materially affected by any public disclosure: the late filing may therefore limit the scope of enforceable method-of-use claims. This sequencing gap directly motivated the explicit placement of Stage 2 as a pre-disclosure step in the model. Future applications should ensure that both trademark and method-of-use patent filings are completed before clinical trial registration and any other public disclosure of the new indication.

3.4 Stage 3: Validation through a Phase IV study

The study was registered on ClinicalTrials.gov (NCT05221892) and conducted at a single accredited centre in Rio de Janeiro. Design: Phase IV, randomized, double-blind, parallel groups, single-centre.

From 451 volunteers screened, 335 were randomized: Group A (n = 170) and Group B (n = 165, standardized dry extract of *Zingiber officinale*, 160 mg/8 mg gingerols – the only herbal medicine registered by Anvisa for motion sickness at the time). Each participant completed four real trips on urban transport (≥ 15 minutes); Trip 1 was without medication (baseline); Trips 2–4 followed oral administration 30 minutes before departure. Primary outcome: reduction of ≥ 20 points on the MSAQ (Motion Sickness Assessment Questionnaire, 16 items, validated).

The primary endpoint was the percentage of patients achieving a ≥ 20 -point reduction in the total MSAQ score relative to the medication-free baseline trip. Group A was superior to Group B at every assessed trip: 54.1% versus 43.6% at Trip 2, 62.3% versus 50.9% at Trip 3, and 66.4% versus 55.1% at Trip 4 ($p = 0.05$ across endpoints). Both regimens were well tolerated; adverse events were more frequent in Group B (77 events) than in Group A (45 events), were predominantly gastrointestinal, and no serious adverse events were recorded. Full results, including secondary endpoints, are reported in the primary clinical publication [17].

3.5 Stage 4: Construction of the regulatory dossier

The regulatory dossier leveraged the existing Anvisa file for the parent product – CMC documentation, manufacturing certification, stability data, and pharmacovigilance records – and supplemented it with the scoping review from Stage 1 (SORT Level B) and the clinical study from Stage 3 (SORT Level A). Core components included an updated package insert with the motion-sickness indication, updated dosage (1 tablet 30 minutes before exposure) and contraindications, updated labelling, and a Technical-Scientific Opinion based on RDC 24/2011. The dossier was submitted to Anvisa on 24 July 2023 (Process No. 25991.006003/77), within the 60-month period established by RDC 242/2018.

In Brazil, Stage 4 is processed through clone registration (RDC 954/2024): a new commercial identity registered under the same technical dossier as the parent product, with the new indication added. Anvisa evaluates only the incremental evidence for the new indication, operationalizing the principle of incremental evaluation. The clone registration dossier for the spin-off is being prepared for submission through Anvisa's SOLICITA system following trademark grant. The Technology Readiness Level trajectory has progressed from TRL 5 (registered product without formal validation of the new indication) to TRL 7

(Phase IV published, dossier submitted, trademark granted, patent filed), with TRL 8–9 (regulatory approval and commercial launch) projected within 12 months.

4. Discussion

4.1 Replicability conditions

The model's replicability rests on four verifiable preconditions assessable before significant investment: (i) a registered pharmaceutical product with a documented, clean safety profile and accepted CMC documentation; (ii) active compounds with demonstrable therapeutic potential for the candidate indication based on existing literature (assessed in Stage 1); (iii) a feasible Phase IV study with respect to patient population, comparator, validated outcome instruments, and ethical/regulatory approvals; and (iv) internal or contracted intellectual property, regulatory, and legal capacity in the target jurisdiction.

Stage 1 functions as the model's investment control mechanism: its output either confirms the investment rationale in Stages 2 to 4 or identifies gaps that need to be addressed before committing resources to intellectual property filings and clinical research. This early risk assessment distinguishes the model from serendipitous repurposing approaches, in which clinical investigation often precedes systematic documentation of the mechanism of action.

4.2 Structural advantages compared to conventional development

The structural advantages of the model operate at three levels. Economically, elimination of preclinical studies and Phases I–III removes approximately 65–75% of total development costs; the Phase IV investment (typically USD 1–10 million) replaces a programme requiring USD 300–700 million for a new molecular entity [8, 9]. Temporally, clinical development falls from 10–15 years to 2–4 years (Fig. 3); in the programme reported here, the entire four-stage trajectory – from study initiation to regulatory dossier submission – was completed in less than 24 months. Strategically, the model offers mid-sized manufacturers the only viable path to generate their own Level A clinical evidence, regulatory approval for a new indication, and intellectual property protection.

The pre-disclosure positioning of Stage 2 adds a fourth structural advantage absent in previous frameworks: maximization of the effective commercial exclusivity window. Because the repurposing pathway compresses the time between patent filing and market entry, the gap between the 20-year nominal patent term and effective exclusivity is substantially smaller than in conventional development [10, 11].

4.3 Limitations

The model's applicability is limited by four structural constraints. The quality of the safety profile is the most critical: the phase bypass mechanism is scientifically and regulatorily justified only for products with clean and well-documented pharmacovigilance records. A product with a problematic history of

adverse events would face significant obstacles at the ethics committee approval and regulatory review stages. The scope of the mechanism-of-action description is the second constraint: the rationale for entering Phase IV is valid when the mechanism of the new indication involves systems already represented in the existing safety profile; a radically different pharmacological mechanism may require additional bridging studies. The availability of an outcome instrument limits the feasibility of Stage 3: indications without validated endpoints require additional methodological investment before the study can be conducted. Regulatory and intellectual property expertise cannot be generalized: Stage 2 requires specific knowledge of the target jurisdiction's patent legislation; Stage 4 requires specific regulatory expertise for each market.

The programme reported here itself surfaces one execution-level limitation: the trademark was filed before clinical disclosure (in accordance with the model), but the method-of-use patent application was filed in June 2026, approximately 32 months after publication of the clinical study. This sequencing gap motivated the explicit pre-disclosure placement of Stage 2 and underscores that future applications must file both trademark and method-of-use patent prior to any public disclosure of the new indication.

A further limitation concerns the evidentiary status of the model itself: it is derived from a single completed programme. While each stage deliverable is independently verifiable, generalisation across therapeutic areas, product classes, and jurisdictions remains to be demonstrated prospectively.

4.4 Contributions to the literature

The model offers four contributions to the drug repurposing literature. First, an operational translation of theoretical advantages documented since Ashburn and Thor (2004) [4] and reviewed by Pushpakom et al. (2019) [3] into a replicable four-stage methodology with defined deliverables for each step — a level of operational detail not previously offered for a complete repurposing trajectory in the medium-sized company context. Second, explicit formalization of the phase bypass mechanism as an organizing principle, rather than as an implicit observation. Third, the introduction of Industrial Property Protection as a mandatory pre-disclosure stage — absent in previous frameworks — with documentation of the extended effective exclusivity window unique to the repurposing pathway. Fourth, documentation of the trademark–regulatory submission interdependence as a critical operational pathway item.

5. Conclusion

This article presented a four-stage operational model for the drug repurposing of registered pharmaceuticals. The model's main contributions are: (1) operationalizing the phase bypass mechanism, enabling direct entry into Phase IV by leveraging existing regulatory documentation for the parent product; and (2) explicitly positioning Industrial Property Protection as Stage 2 — before clinical investigation and public disclosure — maximizing the scope of patentable claims and the effective window of commercial exclusivity.

The the parent product / spin-off programme illustrates the model and documents its refinement: the trademark was filed before clinical disclosure (in accordance with the model), while the method-of-use patent was filed after publication — a limitation that directly motivated the design of Stage 2 as a pre-disclosure step.

The model is replicable by any pharmaceutical company that holds a registered product with demonstrable mechanistic plausibility for a candidate indication and adequate regulatory and intellectual property capabilities. Its main structural advantage — reducing clinical development investment by 65–75% and time-to-market by eight to twelve years — makes it economically accessible to mid-sized manufacturers, which represent the majority of the pharmaceutical industry. Prospective documentation of Stage 4 regulatory approval and commercial launch will provide the final empirical validation of the complete model.

Declarations

Competing interests, funding, author contributions, data availability, and author identification have been submitted through the corresponding fields of the submission system, in accordance with the journal's double-anonymous peer review policy.

Clinical trial number. ClinicalTrials.gov NCT05221892 (registry: ClinicalTrials.gov; registration date: 3 February 2022).

Consent to participate. Written informed consent was obtained from all individual participants enrolled in the Phase IV clinical study (ClinicalTrials.gov NCT05221892).

Consent to publish. Not applicable. This manuscript does not contain identifying information of individual participants.

Use of artificial intelligence. An artificial intelligence-assisted writing tool (Claude, Anthropic) was used during preparation of this manuscript for linguistic structuring, academic writing support, and formatting. The authors reviewed and edited all content generated with the aid of AI and assume full responsibility for the accuracy, integrity, and originality of the content of this publication. The scientific data, methodology, empirical results, and conclusions presented in this article are entirely the work of the authors.

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Figures

Four-Stage Drug Repurposing Model vs. Conventional Drug Development

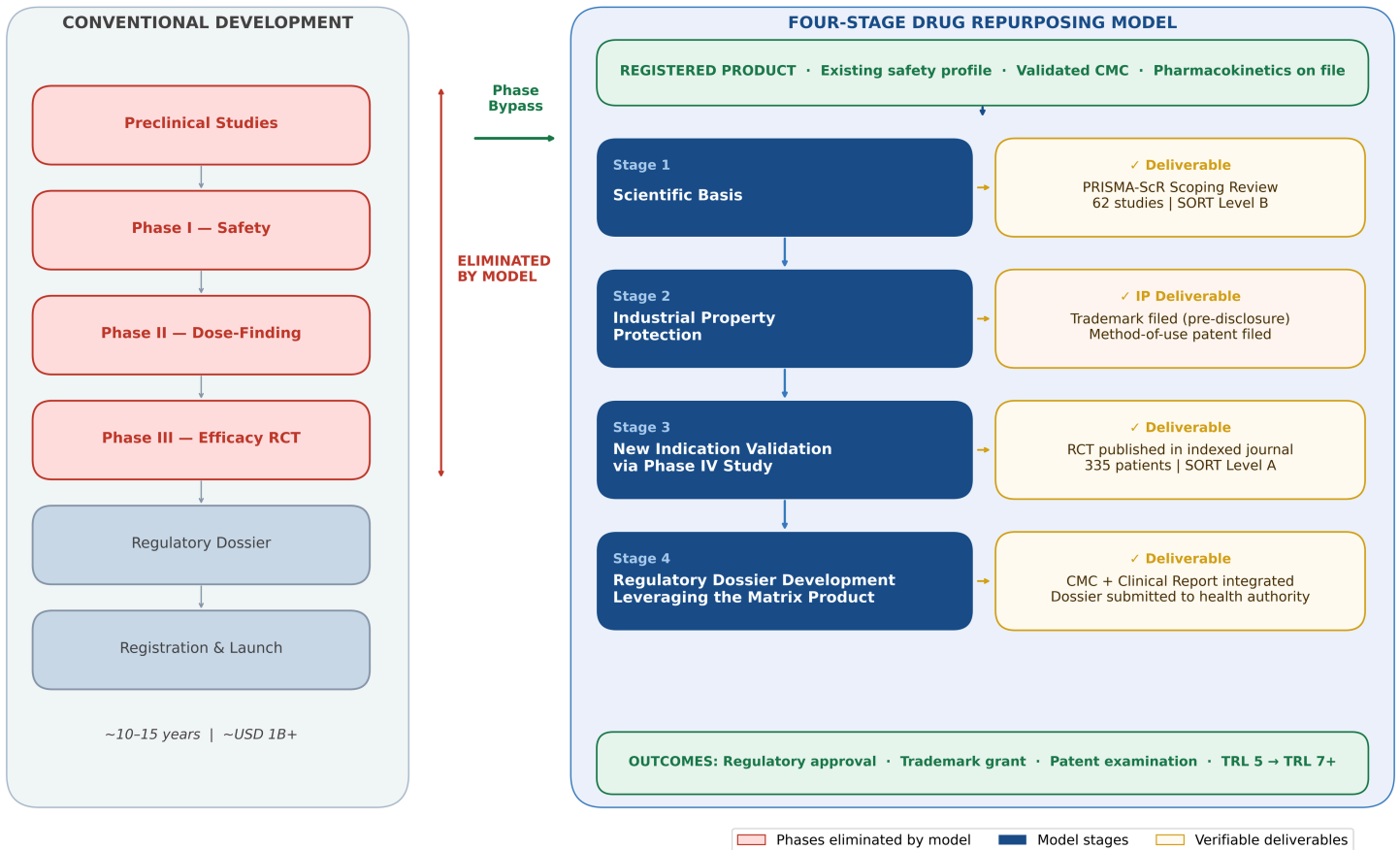


Figure 1

The Four-Stage Model for Drug Repurposing compared to conventional pharmaceutical development

Stage 1 Investment Gate: Scientific Basis Decision Flow

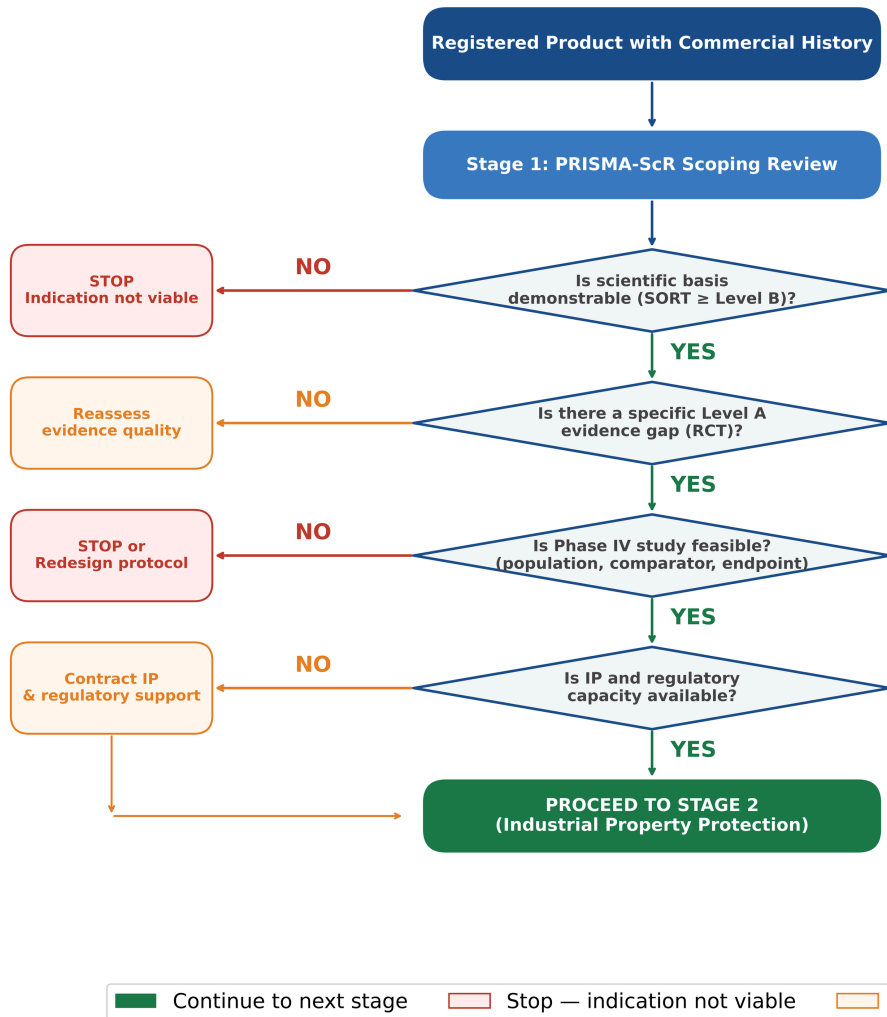


Figure 2

Stage 1 Investment Gate: decision flow for assessing the scientific basis before committing to Stage 2 investment

Development Timeline: Conventional Drug Development vs. Four-Stage Repurposing Model
(Estimated values for illustrative purposes; actual timelines may vary)

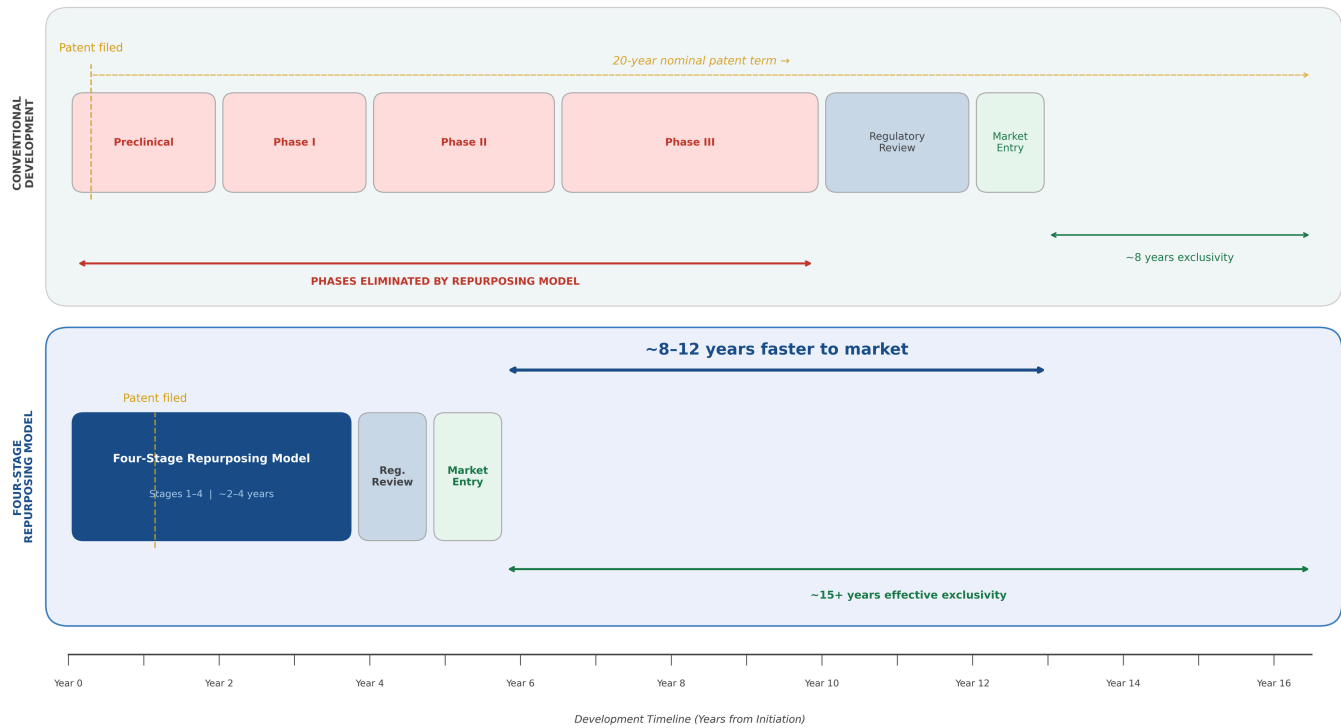


Figure 3

Development timeline comparison between conventional drug development and the four-stage drug repurposing model