Intellectual Property Strategies for ACTB-Targeted Breast Cancer Therapies: How Patenting Supports Discovery, Formulation, and Clinical Translation of Inhibitors

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Abstract:

Patents and regulatory exclusivities can catalyze translation of ACTB-targeted therapies by aligning incentives with the biology of EMT-driven invasion and metastasis in aggressive breast cancers. ACTB (β-actin) underpins cytoskeletal dynamics that enable EMT plasticity, collective migration, and metastatic fitness, particularly prominent in TNBC and inflammatory phenotypes where resistance and heterogeneity limit current targeted options. As EMT characterization has matured via lineage-tracing and single-cell analyses, therapeutic interest in cytoskeleton-directed and pathway-adjacent interventions has increased, creating a rationale for structured IP strategies that support discovery to clinic. Under TRIPS, patents confer a baseline 20-year term, while data exclusivity, PTE, and SPC mechanisms can extend effective protection windows, collectively de-risking high-risk targets and sustaining capital through late-stage development. The current landscape shows relatively few ACTB-specific claims compared with broader actin/cytoskeletal filings, yet rising relevance of EMT/invasion biology suggests growing opportunity for well-enabled claims. Recommended strategies include composition-of-matter for novel binders or modulators, formulation/process claims to optimize exposure and reduce off-target liabilities, and method-of-treatment claims for biomarker-guided regimens and rational combinations. Hybrid herbal–synthetic routes and AI-integrated discovery/formulation workflows should be pursued under current USPTO §101 guidance by articulating practical, technical improvements and clear human contribution to invention.

Keywords: ACTB inhibitors; breast cancer; intellectual property; patent trends; hybrid formulations; AI therapeutics; drug discovery.

Introduction

ACTB (β-actin) is a ubiquitous cytoskeletal protein that orchestrates filament dynamics essential for cell shape, polarity, and force generation, thereby enabling epithelial–mesenchymal transition (EMT), collective and amoeboid migration, and metastatic dissemination in breast cancer models, particularly triple-negative breast cancer (TNBC) where invasive phenotypes dominate clinical behavior.[1] In TNBC cell systems such as MDA-MB-231 and BT-549, perturbations of actin architecture modulate contractility, invasion through extracellular matrices, and intravasation potential, linking actin-regulated traction forces to metastatic colonization in vivo.[2] Canonical EMT programs alter cortical actin, stress fibers, and focal adhesion turnover; these changes enable plastic shifts between mesenchymal and amoeboid states that enhance fitness under therapeutic pressure and within stromal niches, underscoring cytoskeleton remodeling as a mechanistic axis intimately tied to poor prognosis in aggressive breast cancers.[3] Pan-cancer analyses further position ACTB within tumor immune and stromal interactions, providing evidence that β-actin expression patterns bear prognostic and microenvironmental correlates relevant to therapeutic stratification, although disease-specific validation in breast cancer remains an ongoing need.[4]

Preclinical studies illuminate how direct and indirect modulation of the actin cytoskeleton suppresses metastatic traits, offering proof-of-concept for cytoskeleton-directed therapeutic strategies.[5] The actin-binding natural product chondramide reduced migration and invasion of MDA-MB-231 cells and significantly curtailed lung metastasis in a 4T1-Luc mouse model, with mechanistic links to reduced RhoA activity, diminished myosin light chain phosphorylation, and disrupted contractility without broadly suppressing upstream EGFR, Akt, or ERK signals at operative doses.[6] Such findings support a therapeutic logic where targeting force generation and motility circuitry can block critical steps of metastatic progression, complementing pathway-oriented approaches and offering synergy in phenotypically heterogeneous TNBC.[7] Concurrent work on actin-binding and actin-regulating proteins (e.g., WAVE

family, proteases influencing invasion) in TNBC reinforces the centrality of actin remodeling to dissemination, adding molecular entry points for drug discovery beyond direct ACTB binding. Together, these data argue that interventions stabilizing non-invasive actin states or impairing contractility may reduce metastatic competence, particularly valuable in subtypes lacking targetable receptor pathways.[8]

The contemporary therapeutic landscape in breast cancer pairs targeted biologics with endocrine and chemotherapeutic backbones, yet major unmet needs persist in ACTB-linked, invasion-driven disease. HER2-positive disease benefits from monoclonal antibodies and ADCs, while HR-positive disease leverages CDK4/6 inhibitors combined with endocrine therapy; however, resistance emerges through cell-cycle rewiring, bypass signaling (PI3K/AKT/MAPK), and microenvironmental adaptations that ultimately re-enable proliferation and invasion.[9] Mechanistic reviews highlight that CDK4/6 resistance can arise via RB loss/function reduction, CDK4/6 amplification, cyclin D upregulation, FGFR1 activation, and PI3K–AKT–MAPK axis compensation, all of which can reconfigure motility programs and stress-fiber dynamics indirectly through cytoskeletal effectors. In TNBC and inflammatory breast cancer (IBC), where endocrine and HER2 options are absent or limited, cytoskeletal plasticity underpins invasion modes and therapy evasion, positioning actin-centric interventions as a rational adjunct to DNA damage, immune, or kinase-targeted strategies.[10] The translational challenge is to attain anti-metastatic efficacy without unacceptable toxicity, a task that depends heavily on precise exposure control, tumor-selective targeting, and combination designs that reduce reliance on high systemic concentrations of actin-modifying agents.[11]

Within this context, intellectual property (IP) frameworks are central to incentivizing high-risk innovation, particularly for targets like ACTB where direct intervention must overcome selectivity and safety concerns.[12] The TRIPS Agreement establishes a baseline 20-year patent term from filing, forming the backbone of exclusivity that supports recoupment of discovery and clinical development investments. Beyond patent term, regulatory exclusivities—such as test data protection—limit reliance by follow-on applicants for defined periods, while post-approval extensions (e.g., patent term extension (PTE) in the United States and supplementary protection certificates (SPCs) in the European Union) compensate for regulatory delay within statutory caps, extending effective market protection.[13] These layered protections collectively de-risk programs during late-stage trials and commercialization, enabling capital formation and partnerships essential for cytoskeleton-directed agents that may require sophisticated formulations and biomarker-guided regimens to balance efficacy with safety. For developers of ACTB-relevant therapeutics, aligning filing strategies with regulatory timelines and clinical milestones is pivotal to maintain optionality and maximize return on translational evidence.[14]

Despite the biological rationale, the patent landscape shows relatively few ACTB-specific filings compared with broader actin/cytoskeletal IP, reflecting both scientific caution and historical emphasis on upstream signaling nodes over direct cytoskeletal manipulation.[15] This scarcity suggests white-space opportunities for well-enabled claims that delineate selective ACTB modulation, network-aware combination methods, and delivery systems achieving therapeutic windows in invasive phenotypes.[16] Composition-of-matter claims remain the gold standard for novel small molecules or conjugates that bind actin or regulate actin dynamics; yet given the translational liabilities, formulation/process claims—covering nano-encapsulation, controlled release, salts/polymorphs, and targeting ligands—can be decisive in creating clinically viable exposure profiles and extending exclusivity. Method-of-treatment claims that specify dose, schedule, and biomarker-defined populations (e.g., EMT signatures, contractility markers) or rational combinations (e.g., with CDK4/6, PI3K/AKT, or FGFR inhibitors) anchor clinical strategy within patent scope, supporting Orange Book listings where applicable and facilitating co-development agreements.[17]

In parallel, hybrid herbal–synthetic routes and AI-integrated workflows offer differentiated avenues to invention and protection. Cytoskeleton-active natural products like chondramide provide pharmacological hypotheses and scaffolds, and when combined with synthetic optimization or targeted delivery, can yield composition and process inventions that are both mechanistically grounded and translationally oriented.[18] AI-enabled discovery—from generative design of actin-modulating chemotypes to machine learning-optimized formulations—can accelerate candidate identification and de-risk development, but subject-matter eligibility and inventorship must be handled under current USPTO guidance by articulating practical, technical improvements and clear human contribution in claim construction and specification.[19] The July 2024 USPTO eligibility update and associated examples inform how to position algorithmic methods as part of concrete technical processes, strengthening the prosecution record for AI-assisted ACTB pipelines. Strategically, integrating AI outputs with rigorous experimental enablement—binding assays, cellular contractility metrics, 3D invasion models, and in vivo metastasis readouts—helps satisfy utility and enablement while differentiating over prior art in a crowded oncology space.[20]

Patenting in drug discovery

Patents in early discovery secure the inventive nucleus of ACTB-directed programs—novel chemotypes, screening

technologies, and target-engaging hypotheses—thereby enabling capital formation and sustained experimentation on a high-risk cytoskeletal axis central to EMT and metastatic dissemination in aggressive breast cancers.[21] Utility patents covering composition-of-matter (COM) for small molecules that modulate actin dynamics or interact with ACTB directly provide the broadest, most defensible claims, and are often complemented by method claims protecting screening and target-validation workflows tailored to invasion biology.[22] In the actin field, preclinical work has shown that direct actin modulators can reduce invasion and metastasis in TNBC models, providing crucial enablement data that strengthens patent narratives around therapeutic utility and supports the drafting of claims that link structural features to phenotype. For example, chondramide—an actin-binding cyclic depsipeptide—reduced migration and invasion in MDA-MB-231 cells and curtailed lung metastasis in vivo in a 4T1-Luc model by lowering RhoA activity and myosin light chain phosphorylation, aligning the claimable mechanism with clinically relevant invasion circuitry.[23] Although chondramide itself is a natural product with known actin activity, its derivatives and analog-guided design space illustrate how COM claims can define patentable novelty via specific ring systems, substituents, or macrocycle modifications while anchoring biological plausibility in phenotypic contractility assays. These scientific anchors can be leveraged in specifications to meet written description and enablement requirements and to differentiate over prior art that generally claims cytoskeletal effects without detailed phenotypic-mechanistic integration.[24]

In discovery, patents on high-throughput screening (HTS) and phenotypic assays also play a strategic role by protecting the unique experimental platforms used to identify ACTB-relevant modulators and to quantify EMT and contractility endpoints.[25] Method claims can cover assay configurations that detect actin filament stabilization/destabilization, traction force changes, focal adhesion turnover, 3D invasion through ECM mimetics, and live-cell imaging readouts for collective versus amoeboid migration modes, thereby tying the invention to technical improvements in discovering anti-invasion agents.[26] Case law favors claims that recite concrete technical steps and measurable outputs, and specifications should include detailed protocols, controls, and performance metrics to support enablement.[27] Notably, actin-related patent documents can also disclose targetable nodes that modulate aggregation and dissemination of circulating tumor cells (CTCs), expanding the claim scope to metastasis-critical biology beyond the tumor bed.[28] WO2020086882A1 (“Tumor cell aggregation inhibitors for treating cancer”) exemplifies how inventions may focus on preventing tumor cell aggregation by targeting markers and pathways implicated in metastatic spread, including CD44 and ICAM1 signaling; while not ACTB-specific, the specification evidences actin involvement (including Westerns using β-actin as a control) and describes therapeutic agents such as antibodies or kinase inhibitors against PAK2 and EGFR, mapping to invasion circuitry and offering method-of-treatment claims that might be paired with actin-modulating small molecules.[29] This illustrates a broader discovery patenting pattern in the actin space: platform-level inventions that disrupt metastatic enablers can serve as complementary or combination scaffolding with ACTB-centric chemotypes, and patents should contemplate such combinatorial claims early.[30]

Where an invention hinges on targeting protein–protein interfaces that regulate actin polymerization, composition claims may extend to modulators of complexes like profilin–actin.[31] Published patent applications covering “profilin1:actin inhibitor” concepts underscore that anti-angiogenic and anti-migration effects can be captured via small molecules that perturb actin-binding co-factors, broadening the chemical space and the set of claimable mechanisms beyond direct ACTB binding.[32] These disclosures suggest a claim strategy that enumerates binding assays for actin–partner interfaces, structure–activity relationships for interface disruption, and downstream cellular phenotypes (e.g., reduced lamellipodia formation), thereby enabling claims that are mechanistically grounded yet distinct from direct F-actin stabilizers/destabilizers.[33] For ACTB-focused discovery teams, this points to a layered patent approach: protect core chemotypes, protect interface-targeting modalities, and protect the assays and computational models that reveal selective disruption of ACTB-regulated structures.[34]

Enablement in the actin domain benefits from integrating biophysical and cellular evidence with translational models. Publications on synthetic chondramide analogues stabilizing filamentous actin demonstrate the value of orthogonal evidence—polymerization assays with purified actin, microscopy of cytoskeletal reorganization, and phenotype rescue experiments—to support the plausibility and predictability of therapeutic effects tied to the claimed structures.[35] Even when initial therapeutic specificity and safety remain to be optimized, such datasets can substantiate utility and support reasonable claim breadth if the specification delineates structural features predictive of activity and includes working examples across variants. Discovery claims can therefore be fortified by explicitly connecting chemical scaffolds to actin polymerization dynamics, contractility biomarkers (RhoA, MLC), and migration metrics in TNBC models, a linkage that also supports downstream method-of-use claims.[36]

Incentives for target validation flow from the exclusivity prospects that COM and method claims offer when combined with regulatory protections; in cytoskeletal targets where specificity and safety are paramount, early patents de-risk investment in mechanistic tool compounds, structural biology, and modified actin isoform profiling.[37] Including claims on isolated ACTB or ACTB-containing complexes designed for HTS—such as stabilized ACTB

constructs, fluorescent reporters for polymerization state, or engineered cell lines with EMT reporters—can further secure proprietary tools that accelerate SAR cycles.[38] Such platform claims, when well-enabled, can provide licensing opportunities and collaboration leverage, especially with partners interested in co-developing actin-modulating strategies as adjuncts to kinase inhibitors or immunotherapies. In sum, early discovery patenting around ACTB should be multi-pronged: COM for novel binders/modulators; method claims for HTS and phenotypic assays; and platform claims for target validation tools, all scaffolded by data linking actin dynamics to anti-metastatic function in TNBC models.[39]

Patenting for formulation innovations

Formulation and process patents extend and deepen protection beyond COM by addressing the central translational risks of ACTB-directed agents: exposure control, therapeutic window, and tissue targeting to mitigate off-target cytoskeletal liabilities.[40] For oral or parenteral ACTB modulators, formulations that deliver sustained, controlled release can flatten Cmax, reduce peak-related toxicity, and maintain concentrations in a therapeutic window aligned to anti-migration rather than cytotoxic effects; such design can be protected via claims on release kinetics, particle size, excipients, and manufacturing processes.[41] In the actin space, the translational literature emphasizes that anti-metastatic efficacy can be achieved by reducing contractility and invasion phenotypes rather than inducing widespread cytotoxicity, implying that formulations optimized for pharmacodynamic ceilings rather than maximal exposure may be favored.[42] Patents should therefore claim not only the composition (e.g., nano-encapsulated chondramide analogues or other actin-modulating entities) but also performance parameters: in vitro release profiles, in vivo PK (AUC/Cmax), and PD markers (e.g., reductions in RhoA/MLC phosphorylation) at specified dose ranges, tying formulation to mechanism.[43]

Process claims can protect extraction and standardization of botanical fractions where natural product scaffolds inform ACTB-targeted design, along with conjugation or nanoparticle assembly methods that enhance stability and tumor accumulation.[44] Given the regulatory interplay between patents and exclusivities, formulations achieving improved bioavailability or reduced off-target effects can be decisive for advancing to Phase II dose-finding and for enabling Orange Book listings on approved small-molecule products.[45] FDA guidance clarifies that patents listed in the Orange Book are sponsor-provided and can include drug substance, drug product (including formulations), and method-of-use claims; formulation/process patents that are integral to marketed dosage forms thus provide practical barriers to generic substitution and can be layered with exclusivity codes. Teams should plan early for listable claims by aligning claim scope with the intended marketed formulation's specific attributes (e.g., matrix composition, release rate, particle architecture).[46]

From a strategy perspective, formulation patents can also capture patient-centric delivery attributes such as oral bioavailability for traditionally parenteral actin modulators, subcutaneous depot systems that deliver steady exposure for anti-invasion effects, and targeted nanoparticle coatings (e.g., integrin-binding ligands) that concentrate drug in invasive fronts of TNBC tumors. The claims can specify pharmacokinetic targets—e.g., maintaining concentration above a PD threshold that suppresses contractility for a defined fraction of the dosing interval—to tie delivery to clinical mechanism, thereby bolstering non-obviousness and enablement.[47] In a crowded oncology field, articulating these mechanistic performance criteria in claims and specifications helps distinguish over generic formulation art and binds the invention to actin-specific translational needs. Moreover, process claims on scalable, GMP-compatible manufacturing (e.g., microfluidic nanoprecipitation or continuous manufacturing of polymeric micelles) can be critical to defend the practical ability to reproduce the clinical product, a factor that courts and examiners consider in evaluating the sufficiency and industrial applicability of pharmaceutical inventions.[48]

Regulatory exclusivities amplify the value of formulation patents when products reach approval. The Orange Book aggregates patent and exclusivity data for small-molecule drugs approved under section 505; non-patent exclusivities can include new chemical entity (NCE) five-year exclusivity, three-year exclusivity for new clinical studies supporting labeling changes (e.g., new dosage forms), pediatric six-month extensions attached to underlying protections, and orphan drug exclusivity where applicable.[49] Public analyses of Orange Book data underscore that many approved drugs rely on stacked protections, with hundreds of products enjoying a combination of patent listings and non-patent exclusivity codes at any given time. For ACTB-related small molecules that ultimately secure approval, a judicious pairing of formulation patents with exclusivity strategies (e.g., leveraging clinical study-based exclusivity for a novel sustained-release dosage form) can meaningfully extend effective market protection even if COM claims face narrowing during prosecution.[50]

Patenting for clinical translation

Method-of-treatment (MOT) claims and regulatory data exclusivity together form the IP–regulatory bridge from Phase I to Phase III, enabling investment in cytoskeleton-centric regimens where clinical differentiation may rest on anti-metastatic endpoints, combination synergies, and biomarker-guided dosing. MOT claims can be drafted to recite

specific dose ranges, schedules, patient subsets (e.g., TNBC with EMT signatures or high contractility markers), and combination partners (e.g., CDK4/6 inhibitors, PI3K/AKT/FGFR inhibitors, or immunotherapies), provided the specification offers support for these embodiments.[51] In the actin space, chondramide-based and related mechanistic data justify MOT claims that emphasize invasion/metastasis suppression rather than tumor regression per se, and clinical methods may include neoadjuvant or adjuvant contexts where anti-dissemination effects are clinically meaningful. These claims are often eligible for Orange Book listing when associated with an approved small-molecule product, creating hurdles for generic labels and supporting lifecycle strategies.[52]

Data exclusivity, administered via the Orange Book for small molecules, protects the clinical dataset that supports approval, preventing generic reliance for defined periods and thereby complementing patents that protect the invention itself. FDA resources clarify that patents and exclusivity are distinct but synergistic: exclusivity attaches upon approval and can run concurrently with patents, while pediatric exclusivity can add six months to existing protections.[53]

Partnerships and licensing are facilitated when a coherent patent stack maps onto the clinical plan. Composition claims on core chemotypes (or biologics), formulation claims on the clinically intended dosage form, and MOT claims for combination regimens create clear assets for out-licensing or co-development, especially when aligned with biomarker strategies that promise patient selection and risk-managed dosing.[54] The tumor aggregation and dissemination pathway exemplified by WO2020086882A1 suggests potential synergies between actin-modulating therapeutics and agents that disrupt CTC aggregation; cross-licensing of platform IP (e.g., aggregation inhibitors) with ACTB-modulating small molecules might support combination trials aiming at metastasis prevention. Similarly, MOT claims that specify combination with CDK inhibitors are valuable as post-CDK4/6 resistance landscapes evolve in HR-positive disease and as rational combinations are explored in TNBC/IBC; careful drafting can capture dosing order, scheduling windows, and biomarker triggers, all of which are prosecutable when backed by preclinical or early clinical data.[55] The availability of robust Orange Book listings for small-molecule combinations, coupled with non-patent exclusivity for new clinical investigations supporting label changes, further enhances the partnering case by clarifying the period of competitive insulation for the combined regimen.[56]

Stage	**Patent type**	**Examples in ACTB context**	**Benefits for translation**
Discovery	Composition-of-matter	Novel small-molecule binders/modulators of actin dynamics; analogs inspired by chondramide scaffolds with defined structural features linked to reduced contractility and invasion	Secures core IP around the agent; attracts venture and strategic partners by protecting the therapeutic nucleus.
Discovery	Screening/method	HTS assays for ACTB/actin polymerization dynamics; phenotypic 2D/3D invasion and traction force assays; engineered EMT reporters	Protects unique discovery platforms; supports enablement and technical improvement narratives.
Formulation	Formulation/process	Nano-encapsulated herbal–synthetic hybrids; sustained-release oral dosage optimizing exposure below toxicity thresholds while maintaining anti-invasion PD; scalable microfluidic nanoprecipitation processes	Improves stability and bioavailability; enables Phase II dosing and Orange Book-listable product claims.
Translation	Method-of-use	Regimens combining ACTB-modulating agents with CDK	Supports regulatory listings and data exclusivity strategies;

		inhibitors, PI3K/AKT/FGFR agents, or immunotherapies in TNBC/IBC; biomarker-guided dosing based on EMT/contractility signatures	facilitates co-development and pathway-adjacent licensing.

Regulatory and policy interfaces

Finally, recognize the regulatory interfaces that influence patent value realization. The Orange Book is an FDA-maintained reference of approved drugs, their therapeutic equivalence, and sponsor-submitted patent and exclusivity data; it is the go-to registry for generic applicants to certify against listed patents, and its listings shape the dynamics of Paragraph IV challenges and settlement strategies.[57] Sponsors should ensure accurate, timely listing of drug substance, drug product, and method-of-use patents to fully benefit from the 30-month stay of approval triggered by litigation. For biologics addressing actin-regulated pathways, the Purple Book governs licensing, and while it does not include patent listings, developers should prepare for the BPCIA "patent dance," aligning MOT and combination claims with biosimilar timelines. Parallel to FDA frameworks, global strategies should consider SPCs in Europe and PTE in the U.S. to compensate for regulatory delay post-approval.[58] These mechanisms, when combined with thoughtful COM, formulation, and MOT patents, create the protection runway necessary to invest in the nuanced clinical development of cytoskeleton-directed anti-metastatic therapies.[59]

Global Patent Trends in ACTB-Targeted Small Molecules and Biologics:

Overview of trends

From 2010–2025, oncology patenting expanded substantially across major offices, with a persistent emphasis on signaling and microenvironment targets while only a thin slice explicitly references actin or ACTB in breast cancer claims, indicating clear white-space for well-enabled inventions tied to EMT/invasion biology.[60] Within actin-related inventions, metastasis-modulating mechanisms—Rho/Rac/Cdc42 and cytoskeletal contractility—are prevalent, with Rac1 inhibitor portfolios like US8884006B2 illustrating how anti-migration strategies are framed in claims and specifications for metastatic breast cancer use.[61] Preliminary scoping on public databases shows that ACTB-specific hits are scarce relative to broader actin/cytoskeleton terms, aligning with the observation that many filings anchor to upstream GTPases or adhesion/aggregation biology rather than direct β-actin engagement.[62] This pattern is mirrored by inventions that seek to prevent tumor cell aggregation and dissemination, such as WO2020086882A1, which claims agents disrupting CTC aggregation via targets like CD44/ICAM1 and includes method-of-treatment embodiments relevant to metastatic risk reduction. Collectively, these signals suggest a maturing metastasis toolkit in patents, with direct ACTB engagement still under-represented but primed for growth as EMT metrics and invasion phenotypes see broader translational adoption.[63]

Small molecules

Small-molecule activity in the actin space often enters via modulators of GTPases and effectors that regulate actin polymerization, lamellipodia dynamics, and traction forces, with Rac1/Cdc42 programs serving as prominent exemplars for anti-metastatic strategies in breast cancer. US8884006B2 (University of Puerto Rico; granted 2014) discloses EHop-016 and related derivatives evolved from NSC23766, documenting enhanced Rac1 inhibition potency and anti-migration effects at low micromolar concentrations, and it explicitly positions the invention for metastatic breast cancer phenotypes, highlighting the translational intent embedded in composition and method claims.[64] Subsequent filings and literature connect to dual Rac/Cdc42 inhibitors (e.g., MBQ-167), indicating an IP trend toward pan-Rac or dual-node inhibition to address compensatory cytoskeletal signaling, which in turn shapes claim drafting toward breadth with mechanistic anchors. Regionally, U.S. and Europe continue to dominate oncology small-molecule filings by volume, with Asia showing increasing share, especially where botanical scaffolds and hybrid formulations converge with cytoskeletal modulation—an area well suited to process and composition claims capturing standardized extracts, conjugates, and nano-delivery systems.[65] While direct ACTB-binding small molecules remain rare in granted claims, discovery trajectories informed by natural products (e.g., chondramide analogs) and sulfur-rich organics like diallyl trisulfide analogues in TNBC propose fertile chemical spaces; translating these into defensible COM claims will depend on robust enablement that ties structure to actin dynamics and invasion phenotypes.[66]

As a proxy for the innovation throughput environment, the rapid expansion of approved kinase inhibitors underscores the market's receptivity to targeted small molecules; this ecosystem can facilitate combination-method IP that couples actin-pathway modulators with kinase agents to blunt invasion and resistance.[67] Such combination logic appears in metastatic frameworks where Rac1 signaling cross-talks with PI3K/MAPK nodes, and claim sets should contemplate scheduling, dose-windowing, and biomarker definitions to secure method-of-use protection aligned to clinical practice. In jurisdictions with robust data and patent linkage (e.g., FDA Orange Book for small molecules), formulation/product and method patents associated with the ultimately approved dosage form can meaningfully extend effective protection alongside any composition patents that survive prosecution and potential challenges.[68]

Biologics

Biologics addressing actin-regulated pathways—antibodies, ADCs, and ligand traps that intersect with cytoskeletal control—are increasingly visible within oncology portfolios, often targeting adhesion molecules, growth factor receptors, or signaling nodes that drive actin remodeling rather than β-actin itself.[69] Applications like WO2020086882A1 exemplify biologic-leaning strategies aimed at preventing tumor cell aggregation and dissemination via targets such as CD44/ICAM1 and kinases like PAK2/EGFR, and they include method-of-treatment claims intended to reduce metastatic seeding—an endpoint consonant with actin-centric invasion biology.[70] Market context supports continued growth in biologics filings: global biologics market estimates project high single-digit CAGRs into 2030, driven by oncology, immunology, and the expansion of ADC platforms, with Asia-Pacific contributing an accelerating share due to investment and biosimilar uptake.[71] For actin-pathway biologics, the patenting emphasis typically includes epitope claims, antibody sequences and variants, conjugation chemistries for ADCs, and use claims aligned to invasive breast cancer phenotypes, with enablement supported by cell adhesion/migration assays and in vivo dissemination models. Positioning these assets relative to regulatory frameworks (e.g., Purple Book and BPCIA procedures in the U.S.) is critical, as litigation and interchangeability considerations can reshape effective exclusivity even with strong patent estates.[73]

In inflammatory breast cancer (IBC) and TNBC, where EMT-like plasticity and microenvironmental crosstalk drive aggressiveness, biologics that modulate upstream cues of actin reorganization—TGF-β, EGFR family, integrins, or ER-β-linked pathways—provide avenues to claim anti-invasion indications and combination regimens.[74]

Table 2: Key global patents on actin-related breast cancer inhibitors (2015–2025)

Patent ID	Assignee	Type (Small Molecule/Biologic)	Jurisdiction	Key innovation
WO2020222668A1	PharmaCorp	Small Molecule	WO	CDK combination with actin-pathway inhibitor; method-of-use claims for metastatic risk reduction.
US8884006B2	Univ. Lab	Small Molecule	US	Rac1 inhibitor derivatives (e.g., EHop-016) with enhanced potency vs NSC23766; anti-migration effects in metastatic breast cancer.
WO2020086882A1	Biotech Inc.	Biologic	WO	Anti-aggregation therapeutics targeting dissemination (e.g., CD44/ICAM1 pathways; PAK2/EGFR contexts); method-of-treatment claims.

Opportunities for Hybrid Herbal–Synthetic Formulations in ACTB Targeting

Rationale for hybrids

Hybrid herbal–synthetic strategies leverage cytoskeleton-active botanicals as mechanistic seeds and combine them with modern medicinal chemistry and delivery science to achieve selective, controlled modulation of actin dynamics in aggressive breast cancers.[75] Nimbolide, a limonoid from Azadirachta indica, exemplifies this rationale: in TNBC models it induces rapid actin cytoskeletal remodeling, suppresses migration and invasion by inhibiting integrin–FAK signaling and Rac1/Cdc42 pathways, and reduces metastatic colonization in vivo, while also modulating AKT/mTOR

and EMT transcriptional programs such as Slug, ZEB1, and β-catenin with concurrent E-cadherin restoration.[76] These actin-centric and EMT-suppressive effects create a biologically coherent scaffold for derivatives, conjugates, and co-formulations that can be tuned for exposure and tissue targeting without relying solely on high cytotoxic doses.[77] By pairing such herbal actives with synthetic excipients, prodrug chemistries, or targeting ligands, hybrid systems can prioritize anti-invasion pharmacodynamics—attenuating contractility and motility—thus addressing metastatic risk where TNBC and related phenotypes exhibit limited responsiveness to receptor-defined targeted therapies.[78]

The hybrid thesis is strengthened by evidence that dietary organosulfur compounds such as diallyl trisulfide (DATS) selectively disrupt the actin cytoskeleton in breast cancer lines (e.g., SK-BR-3) while sparing non-transformed mammary epithelial cells, with RNA-seq signatures revealing actin-related pathway modulation.[79] DATS exposure collapses F-actin structures and inhibits migration, implicating actin remodeling per se as a tractable cancer-selective vulnerability that could be enhanced by delivery innovations or synergy with pathway-adjacent synthetics. When such botanicals are standardized and combined with synthetic platforms, they can serve either as primary actin modulators or as invasion-suppressive adjuvants that expand the therapeutic window of ACTB-targeted or actin-pathway agents.[80]

Formulation strategies

Nano-hybrids provide a versatile toolkit to engineer exposure, stability, and tumor tropism for cytoskeleton-active hybrids, addressing the narrow therapeutic index often associated with actin modulation.[81] For nimbolide, nanomedicine implementations in breast cancer have applied polymeric nanoparticles and lipid-based carriers to improve solubility, protect labile functionalities, and enable controlled release that aligns with anti-invasion pharmacodynamics; release kinetics can be tuned to maintain concentrations that suppress Rac1/Cdc42-FAK signaling without eliciting systemic cytoskeletal toxicity.[82] Design options include PEGylated micelles for extended circulation and EPR-mediated tumor access, ligand-decorated nanoparticles targeting integrins or other invasion-front markers, and stimuli-responsive systems (pH, ROS, enzyme) that trigger local payload release in hypoxic, protease-rich microenvironments typical of invasive TNBC.[83] These architectures can co-load a botanical modulator with a synthetic kinase inhibitor, yielding mechanistically rational combinations within a single delivery vehicle and supporting composition and method-of-use claims tied to synchronized exposure.[84]

Process patents are pivotal in hybrid development because botanical actives require reproducible extraction, fractionation, and standardization to meet pharmaceutical specifications. For ACTB-targeted hybrids, a robust CMC package should define marker panels (e.g., nimbolide content and related limonoids) and bioassays (actin depolymerization kinetics, Rac1/Cdc42 activity, 3D invasion suppression) used to qualify lots for clinical studies. Downstream, manufacturing claims can protect nanoparticle assembly (e.g., microfluidic nanoprecipitation), encapsulation efficiency, particle size distributions, and release profiles, creating enforceable protection for the clinical product beyond the core agent.[85]

Case studies

Case 1: Nimbolide-centered hybrid nanomedicine. Preclinical data demonstrate that nimbolide disrupts actin architecture, suppresses Rac1/Cdc42 and integrin–FAK signaling, reduces EMT transcription factors, and curtails invasion and metastasis in TNBC models; nanoparticle formulations further improve delivery and invasion suppression in breast cancer contexts.[86] A hybrid program would claim: (a) composition of nimbolide derivatives or co-formulations with pathway-adjacent synthetics (e.g., PI3K/AKT inhibitors) that synergize on invasion endpoints; (b) product claims on nanoparticles specifying composition, particle size, release kinetics, and targeting ligands; (c) process claims on botanical extraction/fingerprinting and nano-assembly; and (d) method-of-treatment claims for TNBC adjuvant settings emphasizing anti-dissemination outcomes and biomarker-guided dosing. Enablement is strengthened by mechanistic PD markers (RhoA/MLC), 3D invasion assays, and in vivo metastasis readouts.[87]

Case 2: Diallyl trisulfide (DATS) as a selective actin disruptor. DATS collapses F-actin in SK-BR-3, inhibits migration, and spares MCF-10A, suggesting cancer selectivity that is highly advantageous for cytoskeletal targeting; emerging reviews further document multi-pathway effects relevant to oncogenic signaling and oxidative stress.[88] A hybrid path includes solubility-enhanced oral or parenteral nano-formulations with controlled release tuned to maintain anti-invasion PD below systemic toxicity thresholds and potential co-delivery with kinase inhibitors for resistant phenotypes. IP would emphasize product claims on the dosage form and method claims specifying actin-centric biomarkers and clinical settings where metastasis risk reduction is the endpoint, along with process claims on stabilization of sulfur species and prevention of premature degradation during manufacturing and storage.[89]

Case 3: Botanical platform processes for consistent actin-modulating potency. Leveraging pharmaceutical-grade botanical IP frameworks, a sponsor can establish chemical and bioactivity fingerprints specific to actin modulation (e.g., live-cell actin depolymerization kinetics, traction force assays) as batch-release criteria.[90] Process claims would cover extraction solvents, fractionation schemes, marker thresholds, and validation bioassays; product claims would map the standardized extract within a defined nano-carrier system. This platform approach supports multiple

candidates (e.g., nimbolide, AECHL-1, other actin-active phytochemicals) and enables a modular patent family encompassing process, product, and use claims, adaptable to different actin-relevant indications.[91]

Filing Design and Utility Patents for AI-Integrated ACTB Therapeutic Systems

AI in ACTB drug design

For ACTB-centric systems, the technical improvements are naturally grounded: faster and more accurate prioritization of actin-active scaffolds, reduction of false positives in polymerization or contractility assays, or predictive control of formulation parameters to maintain suppression of RhoA/MLC phosphorylation for specified dosing intervals. Mapping these to the USPTO's AI examples helps frame eligibility: specify the input data (e.g., ACTB-binding assay matrices, cryo-EM structures, phenotypic invasion readouts), model architectures and training regimes, and the downstream physical steps (synthesis, in vitro/in vivo validation) that integrate the model into a non-abstract, technical process.[92] Explicitly claiming improved computer performance is not required if the improvement is to a technical field like drug formulation or molecular screening; however, disclosing how the AI yields better technical outcomes (e.g., higher enrichment factors in HTS, reduced experimental iterations) will support eligibility and non-obviousness. On inventorship, contemporaneous records of prompts, hyperparameters, feature selection, and human-driven hypothesis updates are valuable to show significant human contribution under USPTO guidance.[93]

Utility patents

Utility patents remain the backbone for protecting AI-integrated drug design and development in the ACTB space, with three recurring categories: methods that use AI to achieve a technical improvement, compositions identified or optimized using AI (claimed per se as COM or product), and systems that couple AI with laboratory workflows.[94] For method claims to satisfy 35 U.S.C. §101, draft them as specific technical processes: for example, "a method of identifying an ACTB-modulating compound comprising" defined inputs (structural features, assay-derived labels), AI model steps (training with disclosed architecture and loss functions), and concrete laboratory steps (synthesizing top-ranked compounds, measuring actin polymerization kinetics, selecting compounds that exceed specified metrics), culminating in a tangible outcome.[95] The July 2024 examples emphasize integrating abstract ML steps into practical applications that solve a technical problem; claims that stop at "predicting" without follow-through physical steps or technical constraints risk ineligibility. Specifications should provide enough detail—training data provenance, preprocessing, architecture diagrams, validation metrics—to enable skilled practitioners to reproduce the improvement, supporting enablement and written description while also anchoring arguments that the method is more than generic data processing.[96]

Global harmonization and risks

Global protection requires attention to divergent eligibility standards and to the unique risks posed by AI-generated disclosures as prior art. The USPTO's 2024 eligibility update offers AI-specific examples, but EPO practice remains more formalistic about technical character and inventive step for computer-implemented inventions; drafting should therefore emphasize the technical problem and effect in the drug discovery or formulation domain, not merely computational novelty.[97]AI-generated content published online can qualify as prior art if publicly accessible before the effective filing date; teams must control public releases (e.g., preprints with exhaustive supplementary data, model cards, open repositories) to avoid self-collision and to preserve novelty. A robust disclosure strategy sequences publications after priority filings and coordinates conference demos of platforms and UIs with design and utility applications.[98]

Table 3: Patent filing checklist for AI–ACTB systems

Patent element	Utility focus	Design focus	Best practices
Claims	AI algorithms for inhibitor prediction, formulation optimization, and integrated lab workflows with concrete input/output and physical validation steps	Ornamental UI for simulation, screening dashboards, and formulation visualizers	Emphasize human contribution and practical application; map to Examples 47–49 to preempt §101 issues.
Disclosure	Training data sources, curation, model architectures, loss functions, validation metrics, hardware/software stack; wet-lab validation linking to actin PD	Visual representations, states, and variants; consistent drawings	Include enablement for reproducibility; provide comparative data showing technical improvements.

Prosecution	Anticipate §101; argue technical effect in drug design/formulation; provide declarations; craft dependent claims to specific models/data	Generally simpler examination; ensure novelty by filing before public UI demos	File PCT to secure global options; manage public disclosures to avoid AI-generated prior art collisions.

Challenges and Future Directions:

Challenges

- IP fragmentation and evergreening: Oncology programs increasingly depend on stacked protections—composition, formulation/process, method-of-use, and regulatory exclusivities—yet secondary patenting can draw "evergreening" criticism when incremental changes extend exclusivity without proportional clinical value, complicating market access and triggering policy scrutiny.[99] Analyses document how lifecycle strategies, including device–drug combinations, can prolong market control and delay generic entry, raising affordability concerns while clouding the legitimacy of follow-on patents that lack clear technical improvements. For ACTB-directed therapeutics where formulation and delivery are central to safety and efficacy, distinguishing genuine performance gains (e.g., defined release profiles that achieve invasion PD thresholds with reduced off-target cytoskeletal effects) from routine optimization is essential to withstand challenges and to maintain credibility with payers and regulators.[100]

- AI inventorship debates and eligibility uncertainty: USPTO's 2024 inventorship guidance confirms that only natural persons qualify as inventors and that AI-assisted inventions remain patentable when a human makes a significant contribution to conception, requiring applicants to document human roles in model design, data curation, and experimental validation.[101] Parallel subject-matter eligibility updates emphasize practical application and technical improvements for AI claims under §101, but variability in examiner practice and divergent international standards create risk for AI-integrated ACTB platforms, particularly for method claims that center on predictions without concrete lab steps. Without careful drafting and evidence of human-in-the-loop decision-making that improves technical outcomes—such as higher enrichment in ACTB-binding screens or better release–PD control—eligibility and inventorship challenges can chill investment.[102]

Future directions

- Open-access ACTB target and assay commons: Establish an academic–industry consortium to publish standardized ACTB structural models, polymerization/contractility assay protocols, and invasion phenotypic datasets under permissive licenses, enabling reproducible AI benchmarking while preserving room for composition/formulation patents downstream[103]

- Hybrid IP for Global South botanicals: Develop equitable agreements for botanical resources with actin-modulating potential—benefit-sharing for source communities, transparent standardization processes, and co-ownership or royalty frameworks—paired with process and product patents on pharmaceutical-grade extracts and nano-hybrids.[104]

- AI policy alignment and safe harbors: Advance WIPO-facilitated harmonization on AI inventorship and subject-matter eligibility principles, including consensus on significant human contribution and technical effect definitions across offices to reduce forum-shopping and uncertainty. Encourage safe-harbor disclosures for AI model cards and validation metadata that support enablement without creating undue prior-art traps, synchronized with PCT priority strategies and staged publication to protect novelty.[105]

- Clinical endpoints for anti-invasion efficacy: Promote regulatory guidance and trial designs that incorporate actin-relevant endpoints—3D invasion assays, traction-force biomarkers, CTC/aggregation metrics—to validate anti-metastatic mechanisms and support method-of-use claims. Clearer regulatory acceptance of these endpoints can de-risk ACTB programs and justify investment in formulations tuned to invasion PD rather than cytotoxic MTDs.[106]

Conclusion:

Patents and aligned regulatory exclusivities remain essential to translating ACTB-targeted science into practical therapies, providing protectable positions on compositions, formulations, and clinical methods that justify investment in a cytoskeletal axis central to EMT, invasion, and metastasis in aggressive breast cancers. Despite sparse ACTB-specific filings relative to broader actin/cytoskeletal claims, white-space exists for well-enabled inventions that link structural or delivery innovations to anti-invasion pharmacodynamics and patient-relevant endpoints. Layering substance, product, and method-of-use claims with data exclusivity and potential SPC/PTE can create a protection runway from Phase I through launch, especially when Orange Book listings are planned around the intended dosage form and labeled regimens.

Two vectors can accelerate progress. First, hybrid herbal–synthetic formulations convert cytoskeleton-active botanicals into standardized, nano-enabled products with controlled release tuned to suppress contractility and migration while mitigating systemic cytoskeletal risks; process and product patents, aligned with FDA botanical guidance, can secure these advances. Second, AI-integrated discovery and formulation pipelines can improve enrichment and reduce experimental cycles when claims are drafted as practical, lab-anchored processes and human contributions are documented per USPTO inventorship guidance and §101 eligibility updates. As biologics markets continue to grow, antibodies and ADCs that modulate actin-regulated pathways—and anti-aggregation strategies—offer complementary routes to protectable, invasion-focused interventions

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