Thomas Lines, Director & CEO

Quercis Pharma – Driving a Paradigm Shift in Next-Generation Anticoagulation with an Anti-Thrombotic, Unleashing the Promise of Isoquercetin and Shaping the Future of Healthcare in 2024 and Beyond

Quercis Pharma, headquartered in Zug, Switzerland, is a privately owned biopharmaceutical company at the forefront of precision medicine and therapeutic innovation. The company strategically focuses on an advanced development pipeline, with a primary emphasis on late-stage clinical studies targeting the prevention of Venous Thromboembolism (VTE) in cancer patients and addressing the specific challenges associated with sickle cell disease.

Distinguished by a commitment to scientific excellence, Quercis Pharma's lead drug candidate stands out as an anti-thrombotic powerhouse. Notably, as it is not a *"blood thinner"* or *"anticoagulant"* but rather prevents coagulation only inside the vascular system, it boasts a significantly lower risk profile for thrombosis and related adverse events when compared to existing treatments, positioning the company as a pioneer in delivering safer and more effective anti-thrombotic solutions.

Beyond its immediate therapeutic pursuits, Quercis Pharma has set its sights on broader horizons. The company strategically plans to extend its impact to encompass cancers and other diseases linked with thrombotic events. In addition, Quercis Pharma is actively advancing a combination drug tailored for both cancer and neurological indications, showcasing its versatility and commitment to addressing unmet medical needs across diverse therapeutic landscapes.

Quercis Pharma was formed in 2019 and purchased various Clinical Stage Assets in development in addition to licensing programs from Harvard University, Western New England University and the Government of Canada.

Thomas Lines, CEO of Quercis Pharma, spoke exclusively to CIO Bulletin about how his company, with a focus on precision, efficacy, and market impact, is hoping to redefine the standards of care and contribute meaningfully to the evolving landscape of therapeutic interventions.

Quercis Pharma: Transforming Therapeutic Frontiers

In 2019, Quercis Pharma strategically acquired Clinical Stage Assets, heralding its entry into the biopharmaceutical domain. Guided by CEO Thomas Lines, the company pioneers a proprietary platform encompassing anti-thrombotic, anti-cancer, neurology and immuno-modulatory treatments.

Within this strategic framework, Quercis Pharma aims to provide innovative, effective, and safe treatments for patients grappling with life-threatening conditions and significant unmet medical needs. Distinguished by a

portfolio featuring orally available Protein Disulfide Isomerase (PDI) inhibitors and Mast Cell Activation Modulators (MCAM's), the company plans to redefine next-generation anti-thrombotics. By turning off the clotting process without thinning the blood, Quercis Pharma hopes to address a critical gap in existing therapies.

With a targeted approach, Quercis Pharma tackles Venous Thromboembolism (VTE) in cancer patients. The promise lies in disrupting the clotting mechanism without elevating the risk of bruising and bleeding. The company's research has shown promising anti-neoplastic effects of PDI inhibitors, propelling a deeper exploration into the contribution of PDI and other pathways to tumorigenesis and metastases.

Quercis Pharma's pipeline developments include the relationship between viral illness and thrombosis. The potential influence of PDI in this context sparks hope for future advancements in thrombosis prevention across multiple diseases.

Quercis Pharma's Vision and Tackling Pharmaceutical Sector Challenges

At the helm of Quercis Pharma's mission is the bold pursuit of transforming the pharmaceutical sector's landscape, specifically in the realms of antithrombotic, anti-inflammatory, and cancer treatments. One of the paramount challenges addressed by Quercis Pharma is the entrenched belief within the industry that every efficacious drug must inevitably come with negative side effects. Dismissing this fallacy, the company, led by CEO Thomas Lines, boldly asserts the potential for a paradigm shift, exemplified by their Isoquercetin based drug candidate, internally known as Kinisoquin™.

In challenging the status quo, Kinisoquin™ emerges as a beacon of innovation with remarkably limited side effects. Dismissing the notion that every medical breakthrough must be accompanied by adverse consequences, the drug demonstrates minimal adverse impact—slightly increased urination, potential slight sleep disturbance if taken post-8 pm, and a notable PDE5a inhibition issue that might elevate libido. For Thomas Lines, the affirmation of the safety of Kinisoquin™ in Quercis Pharma and NIH's Phase 2 studies underscores the potential green light for widespread use.

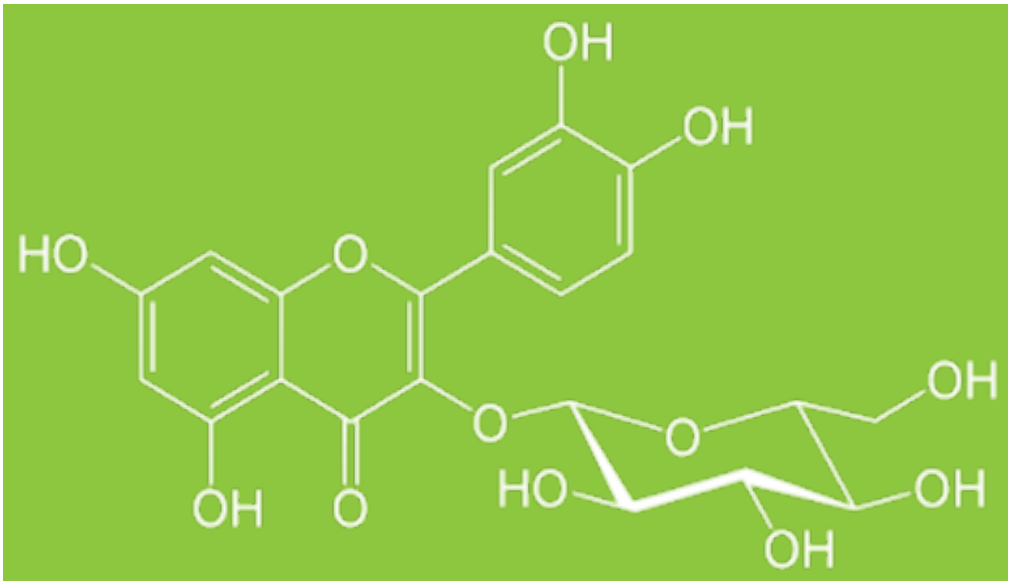
"Our core mission is to stop the world's biggest killer in ALL DISEASES from killing at random in the way it does now - whether it's a heart attack, a stroke, cancer, COPD or viral disease such as Covid 19 - THROMBOSIS is the WORLD's BIGGEST KILLER. We plan to stop it, period!" says Thomas Lines.

Lines further adds, *"Central to this mission are our drugs internally code-named Kinisoquin™ and Kinisoquin FX™, as well as combinations with other PDI inhibitors such as Zafirlukast®, which not only inhibit Protein Disulfide Isomerase (PDI) but also modulate abnormally high secretion of Interleukin 17 (IL17). Both IL17 and PDI play pivotal roles in thrombosis, cancer, neurological diseases, viral replication, and a myriad of human health conditions."* Quercis Pharma stands poised to redefine treatment paradigms, offering a potent arsenal against the world's leading killer—thrombosis.

Kinisoquin™: A Game-Changing Anticoagulant

In the ever-evolving realm of anticoagulation, Kinisoquin™ has emerged as a pioneering contender, offering a novel orally administered anti-thrombotic as opposed to an anticoagulant that stands poised to reshape the prevention and treatment landscape. Distinguished by its unique Mechanism of Action (MoA), Kinisoquin™ effectively intervenes in the clotting cascade, delivering a therapeutic impact without the inherent side effects and bleeding risks associated with existing alternatives.

At the core of Kinisoquin™ lies isoquercetin, a swiftly metabolized quercetin glycoside that transforms into quercetin within the body. This



Kinisoquin™ combination of isoquercetin with vitamins B3 and C

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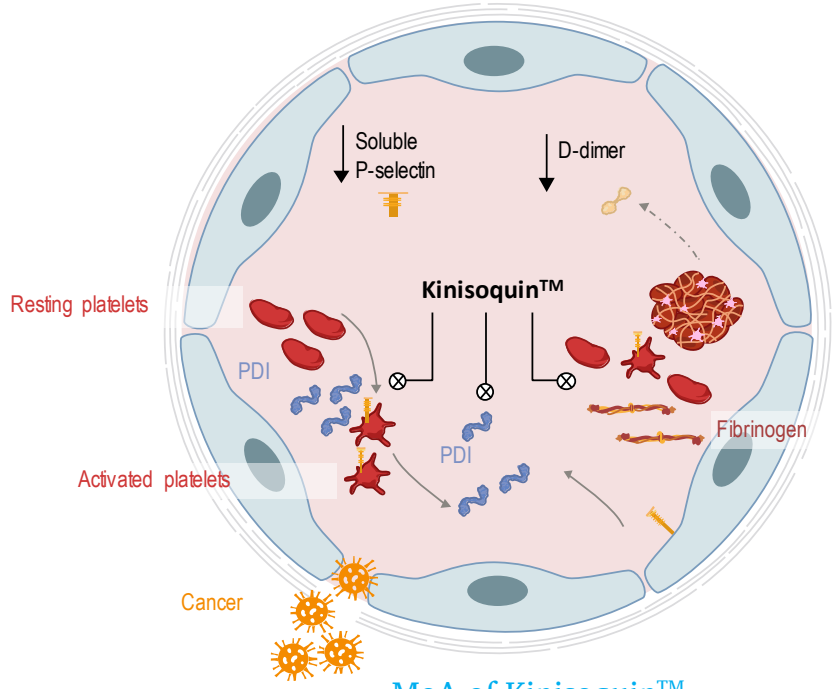

MoA of Kinisoquin™

groundbreaking anti-thrombotic drug goes beyond conventional approaches. In a fixed-dose combination of isoquercetin formulated with vitamins B3 and C, this distinctive formulation not only amplifies bioavailability but has also been shown to improve stability of the investigational drug.

Proven Efficacy: Bridging Lab Discoveries to Clinical Triumphs

Kinisoquin™ doesn't merely make promises; it substantiates them. Its therapeutic efficacy is firmly grounded in rigorous pre-clinical and clinical studies. The Company's investigational drug, has undergone extensive testing in both healthy and diseased human subjects. Over 1,600 individuals have taken isoquercetin in a number of studies with minimal or no toxicity. These studies have uniformly affirmed its safety profile, marking the advent of a new era in anticoagulation therapeutics.

At the heart of Kinisoquin™'s effectiveness lies the inhibition of excessive Protein Disulfide Isomerase (PDI) release into the bloodstream. This pivotal action disrupts the initiation of the thrombo-inflammatory cascade. The consequential result is the inhibition of platelet-dependent thrombin generation, factor 5, 7, 9, 10, 11 and, fibrin formation. Beyond its anticoagulant properties, PDI inhibition emerges as a potential player in diverse arenas, encompassing tumor progression reduction, infectious disease mitigation, and neurodegenerative disease prevention.

The NIH Verdict: A Seal of Safety and Tolerance

In the relentless pursuit of drug development, safety stands as a paramount consideration. A recent study conducted by the National Institutes of Health (NIH) scrutinized the use of Isoquercetin (Kinisoquin™) for thromboinflammation in sickle cell disease. The resounding verdict echoes loudly – Kinisoquin™ was not only well tolerated but also extremely safe, devoid of any adverse events or serious adverse events. This endorsement adds a substantial chapter to Kinisoquin™'s narrative, reinforcing its standing as an exceptionally safe anticoagulant.

Triumph in Phase 2

Kinisoquin™ distinguishes itself as an anti-thrombotic, forging a path distinct from conventional blood thinners. The Phase 2 CATIQ Clinical Trial, a pivotal juncture in Kinisoquin™'s journey, echoed this distinction with a remarkable absence of bleeding, bruising, or drug-associated incidents of thrombosis. The emphatic success of this trial further cements Kinisoquin™'s reputation for exceptional safety.

Charting the Course for Safety in Anticoagulation with an Anti-thrombotic

As the narrative of Kinisoquin™ unfolds, it becomes clear that this novel anti-thrombotic transcends scientific innovation; it stands as

Target product profile: Kinisoquin™ potentially superior alternative to existing anticoagulants, with similar efficacy profile while avoiding common risk of bleeding

	Kinisoquin™	Heparin	DOACs*
Use in cancer associated thrombosis (CAT)	n.a.	Guideline recommend. for **hospitalised patients** mainly and **prophylaxis**[3,4]	Guideline recommend. for **prophylaxis** and **therapy**[4]
		Clinicians are **reluctant to use today's DOACs* and LMWHs*** for **prevention** especially in **non-hospitalised patients**	
Platelet effect	**Inhibits platelet activation**[1]	**Thrombocytopenia**[5]	**Inhibit thrombin induced platelet aggregation**[8]
Route of admin.	**Oral**	**Intravenous injection**	**Oral**
Biomarkers	**58% reduction** of P-selectin[2] **29% reduction** of D-Dimer[2] **58% reduction** of Thrombin generation[2]	**10%** reduction of P-selectin[4] Effects on D-Dimer **inconsistent** Thrombin generation inhibited up to **100%** at 0.5 U/mL	**Effect** on P-selectin not reported[9] **30–40% reduction** of D-Dimer[10] Thrombin generation inhibition: **strong and long** lasting effect[11]
Impact on VTE events	**No primary VTE** in Phase II[2]	**Approx. 60% reduction** of cumulative VTEs[6]	**Approx. 60% reduction** of cumulative VTEs[12]
Bleeding	**No major bleeding** in any clinical study[1]	**1–10%** of patients suffer bleeding[5] **5–6% major bleeding** in CAT prevention[7]	**2-3.5%** in **CAT patients** Approx. **2×** higher than placebo[12]
		Anticoagulant reimbursement levels: $2,000-10,000 yearly* treatment cost per patient	

a beacon of safety and efficacy. From its ingenious composition to its multifaceted Mechanism of Action, Kinisoquin™ signals a new epoch in what used to be anticoagulation, where the specter of bleeding risks is minimized, and safety takes center stage. The resounding endorsements from the NIH Sickle Cell Disease Phase 2 Study and the Beth Israel Deaconess Medical Center at Harvard Medical School led Phase 2 CATIQ clinical trial success underscore that Kinisoquin™ is not merely another over-hyped investigative drug; it heralds a paradigm shift, paving the way for a future where safety and efficacy seamlessly coexist in the realm of anticoagulation.

Road Ahead

In 2024, the CEO of Quercis Pharma, Thomas Lines, is excited to unveil the promising developments that will shape the company's trajectory. The initiation of Phase 3 studies stands out as a pivotal commitment to advancing healthcare solutions under his leadership.

During mid-2024, Quercis Pharma is set to embark on Phase 3 studies with a specific focus on addressing Cancer Associated Thrombosis in Pancreatic and Ovarian Cancer. These studies underscore the company's dedicated efforts to tackle intricate challenges in cancer treatment, particularly in addressing thrombotic complications linked to these complex and debilitating cancers.

Looking forward, Thomas Lines and his team are strategically planning for a Phase 3 study targeting sickle cell disease, scheduled to commence later in 2024. This initiative carries significant weight for Quercis Pharma as it aligns with their mission to contribute to healthcare equity. The objective is to develop an affordable drug that can effectively manage sickle cell disease, especially poignant in light of the recent approval of a CRISPR treatment expected to be priced at a substantial $1.2 million per patient.

In terms of notable milestones, the anticipation is high for an interim readout in Quercis Pharma's Pancreatic Cancer-associated thrombosis prevention study, projected as early as Q1 of 2025. These pivotal moments of insight are deemed crucial as the company navigates the intricate landscape of medical research, all in a dedicated effort to bring impactful solutions to those in need.

"At Quercis Pharma, we stand at the forefront of innovation, driven by a dedication to improving lives and reshaping the future of healthcare. The upcoming Phase 3 studies represent not just a scientific endeavor but a testament to our unwavering commitment to making a meaningful difference in the lives of patients worldwide," concludes Lines.

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