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Quoin Pharmaceuticals (QNRX-NASDAQ)

QNRX: Assessing QRX003 For Multiple Conditions; Opening International NS Clinical Sites

Quoin is optimistic that QRX003 could become the 1st approved treatment for Netherton Syndrome (NS). QRX003 is being evaluated for NS in 2 active studies in the U.S. & QNRX is expanding the clinical trial sites internationally under the IND application, beginning with a center in Saudia Arabia currently treating NS patients who will be eligible to participate in the study.

OUTLOOK

With a strategy to design products to treat multiple indications, QNRX intends to study QRX003 for several conditions & build a database supporting its efficacy and safety as a treatment for a range of dermatological conditions. The company plans to begin a clinical study of QRX003 in Peeling Skin Syndrome (PSS), a rare autosomal disease that has no approved treatment. By developing its assets for multiple indications, QNRX aims to increase the potential for an expedited regulatory pathway, attain economies of scale on R&D, sales & marketing and other costs and potentially broaden the target market if/when commercial sales launch.

Current Price (8/21/24)	$0.58
Valuation	**$2.00**

SUMMARY DATA

52-Week High	**$6.76**
52-Week Low	**$0.47**
One-Year Return (%)	**-89**
Beta	**2.01**
Average Daily Volume (sh)	**45,872**
ADSs Outstanding (mil)*	**4.0**
Market Capitalization ($mil)	**2**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**7**
Insider Ownership (%)	**31**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2024 Estimate	**N/A**
P/E using 2025 Estimate	**N/A**

*Not PF

Risk Level	**High,**
Type of Stock	**N/A**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021					0 A
2022	0 A	0 A	0 A	0 A	0 A
2023	0 A	0 A	0 A	0 A	0 A
2024	0 A	0 A	0 E	0 E	0 E

Loss / Earnings per ADS*

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021					-$5.42A
2022					-$70A
2023	-$4.09 A	-$2.13 A	-$1.95 A	-$2.08 A	-$9.64A
2024	-$1.11 A	-$0.39 A	-$0.44 E	-$0.44 E	-$2.02E

Quarters might not sum due to rounding & share counts

Disclosures on page 17

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AMBITIOUS STRATEGY TO ADVANCE QRX003 FOR MULTIPLE INDICATIONS

International expansion of clinical trial sites for QRX003 study, beginning with Saudi Arabia…

Quoin Pharmaceuticals (QNRX-NASDAQ) has made numerous strides advancing its portfolio of assets to treat various rare and orphaned diseases. The company's lead asset is QRX003, which currently is being evaluated for the treatment of Netherton Syndrome (NS) in two active studies that are being conducted concurrently in the U.S. The company also intends to expand its clinical trial sites for QRX003 internationally under the open FDA Investigational New Drug (IND) application. A center in Saudi Arabia will be the first international location participating in the study. It is currently treating several NS patients who will now be eligible to participate in Quoin's studies. The company has hired an experienced CRO (Clinical Research Organization) to manage its clinical development activities in Saudi Arabia.

The company also intends to expand its clinical activities into several EU countries, as well, and has engaged a European CRO to help with those efforts. Quoin has indicated that plans to add new international venues in the study are at an advanced stage. With five domestic sites open, the company is optimistic that opening international sites will accelerate overall recruitment activities and diversify the patient population being tested.

QRX003 - Potential to Become 1st Approved Treatment for Netherton Syndrome

Quoin is optimistic about QRX003's prospects to be the first approved treatment for NS. There are no approved NS treatments currently and the overall patient population is fairly sizable. Quoin estimates that there are about 6,000-7,000 patients in the U.S. and EU suffering with Netherton syndrome. Data is not readily available and these estimates are within the range of other published estimates. The National Organization for Rare Disorders (NORD) indicates that the actual number of people suffering from Netherton syndrome might exceed the number of reported cases because it is often undiagnosed.

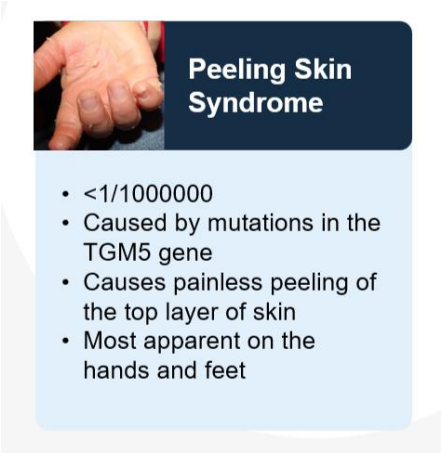
The active ingredient in QRX003 is a broad-spectrum serine protease inhibitor, whose mechanism of action is intended to down-regulate the hyperactivity of skin kallikreins, leading to a more normalized rate of skin shedding. If proven to be safe and effective, long term daily application of QRX003 could lead to the development of a more normally functioning skin barrier and a significant improvement in the quality of life of NS and potentially other patients.

Initiating clinical study in Peeling Skin Syndrome

Moreover, in addition to studying QRX003 to evaluate its safety and efficacy in treating NS patients, Quoin intends to study QRX003 for other conditions and earlier this month announced plans to initiate a clinical study in Peeling Skin Syndrome (PSS) to evaluate the safety and efficacy of QRX003 in New Zealand in a pediatric patient with PSS.

Peeling Skin Syndrome is a rare autosomal disease that has no approved treatment or cure. Quoin believes it has the opportunity to achieve the first regulatory approval for PSS. Most forms of PSS present at birth or during infancy, according to NORD. Symptoms include shedding or peeling of the outermost layer of the skin.

Quoin has identified the first clinical site and patient and is coordinating with the New Zealand venue to initiate clinical testing quickly. The company is also evaluating additional potential sites in other countries. As noted, the company is also evaluating additional opportunities for QRX003.

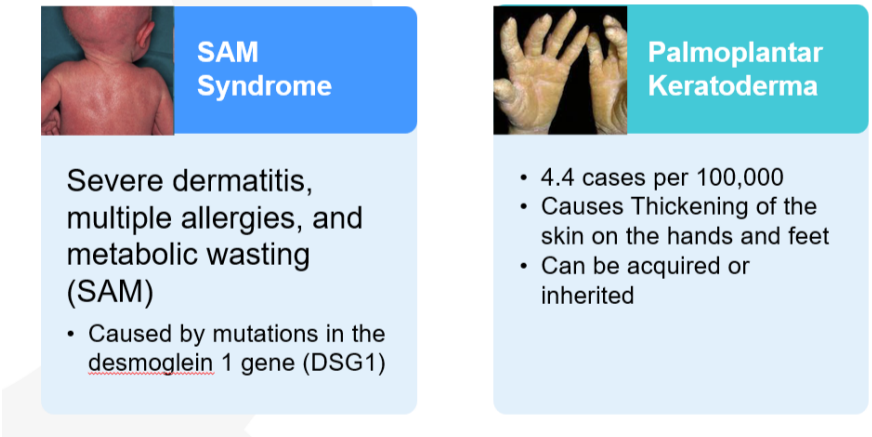


Source: Company presentation

Assessing assets for multiple indications can help spread costs over expanded base…

This initiative is consistent with the company's objective to develop its assets for multiple indications. QNRX is pursuing R&D of its assets for multiple indications, the company expects to build a database supporting the efficacy and safety of QRX003 as a treatment for dermatological conditions. We believe the various studies underway and multiple target conditions could also expand the avenues to potential regulatory approval. The potential for an expedited regulatory pathway is supported by the significant increase in approvals of products to treat rare and orphan diseases in recent years. For example, according to NORD (National Organization for Rare Disorders), 564 orphan products were FDA-approved to treat 838 rare diseases as of January 2020,, of which some 30% received approval in the three years prior.

QRX003 For Additional Rare Skin Conditions



Source: Company presentation

As Quoin's products are being designed to treat multiple indications, lead asset QRX003 is furthest along as a planned treatment for NS, as noted. In addition to the planned PSS study, Quoin has also indicated that it is making progress in providing proof of concept for clinical testing for QRX003 in other indications, including SAM Syndrome and Palmoplantar Keratoderma.

As Quoin expands its clinical activities and potential applications to other patient populations, this strategy is expected to broaden QRX003's target patient populations and commercial prospects, create operating and cost efficiencies and scale and enhance the commercial opportunities of QRX003 and other drugs in the product pipeline. This strategy is also consistent with recent trends in treatments for orphan drug disorders. According to NORD, at least 154 orphan products were approved initially to treat a single rare disease and ultimately earned approval to treat one or more additional orphan indications.

Two active late stage clinical trials in the U.S. for NS running concurrently under open IND

As noted, the company has two active late stage clinical trials in the U.S. for NS that are being conducted concurrently under an open Investigational New Drug (IND) application with the FDA to evaluate lead asset QRX003 for the treatment of NS. One study is a randomized, double blinded, placebo -controlled study designed to assess two different doses of QRX003 topical lotion versus a placebo lotion in NS patients. The second study is investigating the safety and efficacy of QRX003 in Netherton Syndrome patients currently receiving off-label systemic therapy, primarily biologic therapy. The trial is a single arm, open label study investigating the safety and efficacy of QRX003 in these Netherton Syndrome patients, who will continue to receive the treatment throughout the trial. This study is not placebo-controlled.

Preliminary clinical data was positive. Five of six subjects evaluated initially had negligible or absent pruritus (itch) following treatment with QRX003, which represents a substantial improvement for these patients compared to before the study even though all of the subjects enrolled have received off-label systemic treatment for at least one year and/or multiple years. Moreover, all six subjects had positive impressions of QRX003 on multiple metrics that were assessed.

Following initial positive clinical data, the company implemented several protocol amendments to its clinical program to optimize its clinical effort. The company believes these protocol modifications could potentially result in accelerating and/or expanding regulatory approvals for QRX003. The amendments, which had all been cleared by the FDA, include increasing the size of the open-label and blinded studies to 20 and 30 subjects respectively, modifying dosing frequency to twice-daily from once-daily, eliminating the lower dose from the blinded study and reducing the age of eligibility to prospective candidates who are at least fourteen years old.

The company believes this represents the first time that non-adult Netherton subjects will be tested in clinical studies conducted under an open-IND. FDA guidelines for testing non-adult patients are relatively strict. They indicate that developmental treatments should first be studied in adults before being assessed in pediatric populations, defined for medical purposes as patients up to the age of 18 to 21, depending on the trial. Treating pediatric patients is important for a variety of reasons, including that early diagnosis and treatment are important to managing the disease. Moreover, according to NIH, life-threatening complications such as severe cutaneous infections up to sepsis and hypernatremic dehydration “are frequent in infancy.” Quoin notes that newborns with NS have skin that is “red and scaly all over” and “trouble gaining weight in infancy and childhood is common and can be severe.”

The FDA clearance enables Quoin to recruit teenage patients who are currently receiving off-label systemic therapy to participate in the open-label study and those who are not receiving such therapy are not eligible to participate in Quoin’s ongoing placebo controlled blinded study. The company is optimistic that this will not only broaden the pool of people eligible to participate in the studies and therefore facilitate recruitment efforts, but also potentially contribute to the growing database to present for potential regulatory approval; QRX003 is being tested both as monotherapy and in conjunction with off-label treatments. Moreover, given the numbers of younger patients with NS, this could also help shorten the timeline to finding a strong treatment option for this younger patient population. In fact, Quoin believes it is the only development company conducting dual NS studies concurrently under an open IND application. With both trials utilizing the same investigators and clinical sites, Quoin expects to attain substantial operational synergies and cost savings.

With the recent upsize in the number of participants for the two studies, Quoin plans to will test an aggregate of 50 NS subjects. Of those, more than 30 will be treated with QRX003 at the target commercial dose, either as monotherapy or in conjunction with systemic biologics. Quoin is optimistic that once both clinical studies conclude, the data could be sufficient to support an NDA filing so that additional clinical studies in NS subjects will not be necessary.

Moving QRX003 forward in studies as treatment of multiple indications



Source: Company presentation

LEVERAGING M&A, UNIVERSITY AFFILIATIONS TO EXPAND OPPORTUNITIES

School of Pharmacy at University College Cork (UCC) in Ireland…

The company has recently formed a research partnership with the School of Pharmacy at University College Cork (UCC) in Ireland, which management believes has the potential to lead to the development of a number of topical rapamycin (sirolimus) formulations utilizing the university's proprietary dissolvable microneedles technology delivery.

Rapamycin is an immunosuppressive therapeutic drug that has been assessed as a potential topical treatment for a number of rare and orphan diseases. It inhibits the mammalian target (mTOR) cellular signaling pathway but there are numerous challenges that might limit its effectiveness when delivered topically – including the drug's molecular size, extremely poor solubility and other physico-chemical properties.

However, the School of Pharmacy at UCC has had success designing dermal drug delivery technologies, according to QRNX, with a focus on dissolvable microneedles. UCC's dissolvable proprietary microneedles delivery technology are microneedles constructed from a diverse range of biodegradable materials that dissolve rapidly upon skin penetration and are designed to penetrate the skin and release the active pharmaceutical agent. This technology potentially optimizes intradermal drug delivery. At the same time, the company believes UCC's technology could also have several advantages compared to other delivery technologies, including administrating treatment painlessly with minimal skin trauma, reducing the risk of infection, and providing simpler and safer disposal after treatment. The microneedle delivery technology can be used to deliver both large and small drug molecules.

If Quoin and UCC jointly develop successful formulations as potential treatments for several rare and orphan diseases, Quoin intends to move forward with clinical development activities. Quoin will finance research at UCC to assess development of various topical rapamycin formulations for potential treatments for several rare and orphan diseases for which there are no approved therapies or cures. Once the research program is completed, Quoin has the option to advance the clinical development of these rapamycin formulations. Quoin does not need to pay upfront license or milestone fees, nor royalties based on future product sales.

Queensland University of Technology in Australia…

The company also has efforts underway regarding clinical testing of pipeline products with Queensland University of Technology for treatment of Scleroderma and / or NS. Quoin has signed research agreements with the Queensland University of Technology, Australia for the development of a potential treatment for scleroderma and another for NS. Quoin has licensed two assets for development from

Queensland University of Technology: QRX007, also for NS, and QRX008 for Scleroderma. Both of Quoin's dermatological rare disease research programs with Queensland University of Technology for treatment of Scleroderma and Netherton Syndrome continue to move forward and the company is optimistic about clinical testing in Australia, which has the dual benefit of lowering costs via economic incentives and usually generating data that is viewed positively by U.S. and other regulators. Quoin expects to benefit from a 43.5% rebate on all research dollars spent in its Australian clinical testing programs.

By leveraging relationships with universities and other sources, as well as the M&A market, the company seeks both early-stage and late-stage assets that could enhance its overall portfolio and is especially interested in acquiring derisk late-stage assets. Quoin is currently looking at several potential opportunities. The company plans to further expand its existing product portfolio by adding additional assets that address unmet medical needs and is actively looking to bring in additional rare & orphan assets and, at some point, to also expand beyond skin conditions to other categories.

Quoin's recent agreement with UCC is consistent with its goal to expand its product portfolio and opportunities through affiliations with academic institutions and through M&A. Separately, the company has indicated that it continues to evaluate several M&A prospects in rare and orphan diseases that it views as promising, as growth through M&A remains a priority for Quoin.

Strengthening IP portfolio…

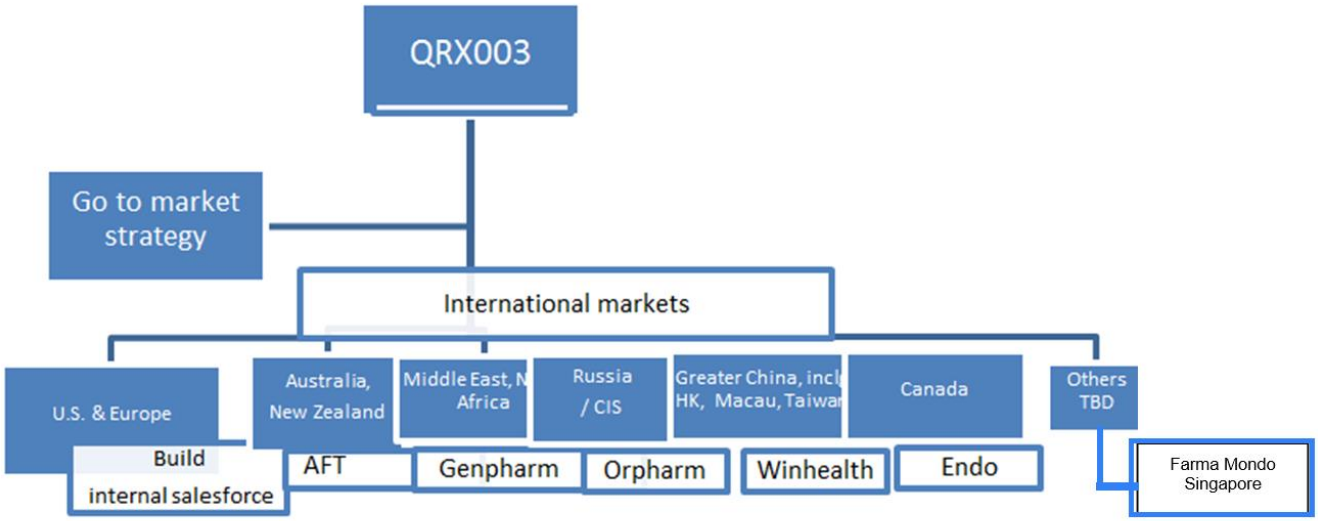
To strengthen its IP position in NS and other orphan / rare disease spaces as it pursues R&D efforts of its assets for multiple indications, Quoin recently filed U.S. and International patent applications for a novel combination product as a potential treatment of NS. This new product combines a broad spectrum serine protease inhibitor with an anti-inflammatory agent in a proprietary topical formulation. Quoin expects that if granted, patents from these applications will extend to at least 2044. At the same time, Quoin continues to explore additional patent opportunities for the product in both clinical and in the manufacturing of the active ingredient and finished product.

Currently, some NS patients are being treated off-label with systemic biologics, including systemic therapy, that provide some symptomatic relief but do not address all symptoms or the underlying cause of NS. The company is optimistic that if the studies are successful, QRX003 for NS could potentially become the standard of care for NS patients. Moreover, with Quoin studies internationally for QRX003 in NS, PSS and potentially other indications, we believe the company is expanding QRX003's prospects for approval, commercialization and future sales.

In addition, the company is working with regulatory consultants to see if QRX003 could qualify for conditional marketing approval in Europe. Conditional marketing approval, which allows for the commercialization of a medical product in advance of formal regulatory approval, is sometimes granted by the EMA when there is no other available treatment for a particular disease when a clearly defined medical need exists.

Sales infrastructure in place…

To prepare for the expect commercialization of QRX003 and other therapies, Quoin is developing an internal sales / distribution infrastructure to cover the U.S. and Europe and has entered into partnerships, for international markets. Quoin has also entered into an exclusive license and distribution agreement with Switzerland's Farma Mondo SA, granting Farma Mondo an exclusive license to commercialize QRX003 in Singapore, once regulatory approvals have been attained.



Source: Zacks from Company reports

Quoin has established a global commercialization and distribution network encompassing at least 60 countries, including Greater China, the Middle East, Canada, Australia and New Zealand and parts of Latin America, Central and Eastern Europe and Turkey, among other markets, with additional discussions underway to extend the commercial applicability of QRX003 and potentially other products. Quoin also continues to work with its partners to explore potential opportunities for the advancement of QRX003 into local Compassionate Use or Early Access Programs in some markets ahead of QRX003 receiving regulatory approval.

Targeting U.S. and EU approvals

Given regulatory actions to facilitate and expedite approval of drugs to treat orphan and rare diseases, Quoin expects the timeline will be relatively short compared to development timelines of drugs to treat more widespread diseases. QRX003 formulation is fully developed and has been manufactured at commercial scale. The company is working closely with supporting foundations and will have access to patient registries, according to management. Quoin also has QRX007 for Netherton Syndrome in development and believes that patients eventually might be able to use QRX007 in combination with QRX003.

The FDA has indicated that that roughly 20 subjects enrolled in its clinical testing and presenting positive evaluations may be sufficient for garnering regulatory approval and Quoin is optimistic that EU regulators might also deem this a sufficient number. Moreover, QRX003 qualifies for at least one (or more) expedited approval pathways and following evaluations of the first several patients enrolled in the ongoing NS studies noted above, the FDA lowered the requirements for achieving a successful clinical outcome.

QUOIN PRODUCT PORTFOLIO & PIPELINE

QRX003

Quoin's initial focus is on dermatological indications. Skin is the body's largest organ and first point of contact for microbes and toxins. Demand for products and therapies to treat dermatological disorders has climbed in recent years, driven in part by the aging of the population, and increased awareness of ways to treat and manage symptoms, beginning largely by focusing on products that treat rare skin diseases, as noted. Quoin has three lead products in development; QRX003 for Netherton Syndrome (NS) is the most advanced.

QRX003 is a topical lotion that is intended to be applied once daily and, in the case of Netherton Syndrome, to the whole body for the remainder of the patient's life. In addition to assessing QRX003 development for treatment of NS and Peeling Skin Syndrome, Quoin also plans to pursue QRX003 for other rare dermatological indications, including potentially SAM Syndrome, and Palmoplantar Keratoderma. Currently, there are no approved treatments for these diseases.

QRX003 contains a broad-spectrum serine protease inhibitor (SPI), which penetrates into the skin and regulates the hyperactivity of certain skin kallikreins that are responsible for the excessive skin shedding that NS patients suffer from and which leads to the highly porous skin that is indicative of the disease. The SPI also acts as a strong anti-inflammatory and antioxidant. QRX003 is formulated with the patented Invisicare® delivery technology, which Quoin licenses from Skinvisible Pharmaceuticals, Inc. Invisicare enables users to apply the product once daily and the treatment remains active on the skin all day without needing to be reapplied. Quoin has the exclusive right to use the Invisicare technology for all orphan dermatology applications, including QRX003, according to management. QRX003's goal is to reduce the patient's skin shedding and help enhance the protective barrier over the skin.

QRX004

QRX004 is a topical lotion that is also utilizes the Invisicare® delivery technology. QRX004 contains two active ingredients and is initially being developed as a potential treatment for RDEB (see below). The primary ingredient in QRX004 helps create robust and sustained type VII collagen that improves wound closure, reduces blistering and generally strengthens the skin.

QRX006

QRX006 is a topical lotion that Quoin is developing to treat a rare disease that the company has not disclosed yet. The existing standard-of-care for this disease generally requires both oral and IV infusion over a prolonged period and many patients have had side effects, according to the company. Quoin believes QRX006 could be a much better treatment alternative that could reduce the side effects and also obviate the need for daily visits to a medical facility for IV infusions.

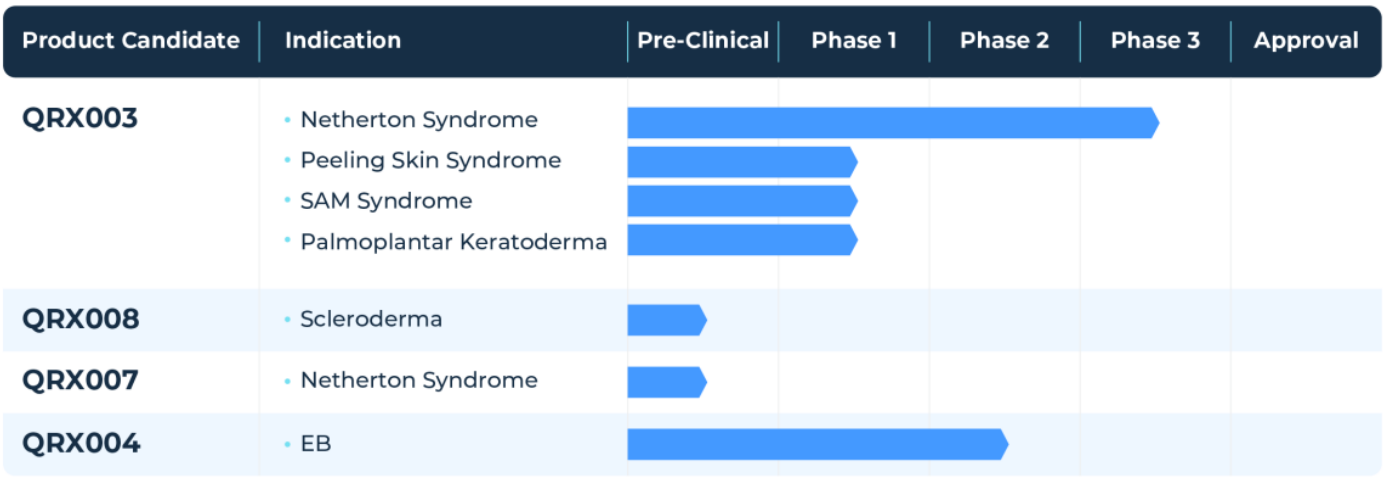
QRX007

Quoin in-licensed QRX007 from Queensland University Technology of Australia. QRX007 is active as a dual domain serine protease inhibitor with proven anti inflammatoryactivity and already in use as a biopharmaceutical for the treatment of acute and chronic pancreatitis, Sepsis and toxic epidermal necrolysis. QRX007 is a human protein and Quoin therefore believes it is highly unlikely to provoke an immune response. A pre-clinical program is underway at Queensland University Technology. Quoin did not pay an upfront fee for the licensing right and has global rights in exchange for a mid-single digit royalty on future sales if regulatory approvals are obtained.

QRX008

QRX008 is the second product that Quoin has in-licensed from Queensland University Technology. It is being developed to treat scleroderma, which is a rare and sometimes fatal autoimmune disease for which no approved treatments currently exist. Scleroderma is caused by an over production of collagen, which results in hardening of the skin and connective tissue. Quoin's focus is on investigating small molecule inhibition of the VCAM-1: VL-4 interaction; there is an established genetic and clinical link for VCAM1 in scleroderma and the pivotal role VL-4 plays in controlling immune cell migration into inflamed tissue. Therefore, the VCAM-1:VL-4 interaction is an attractive target for therapeutic intervention in scleroderma. Proof of concept has already been established in a mouse model and additional studies are underway to select a candidate for clinical testing.

Quoin Product, Development Pipeline



Source: Company presentation EB Epidermolysis Bullosa

RARE & ORPHAN DISASES IMPACT LARGE NUMBERS OF PEOPLE

The FDA defines an orphan disease as one that affects fewer than 200,000 people nationwide. In the aggregate, however, many people suffer from various diseases that are categorized as rare and / or orphan. Orphan diseases impact about 25 million people in the U.S. in the aggregate, according to National Institutes of Health (NIH) data. In 1983, Congress passed the Orphan Drug Act, which provided incentives for biotech and pharma companies to develop new drugs and therapeutic treatments to help people suffering from rare and orphan diseases that Big Pharma might not find meets the level of economic return to warrant development. According to the U.S. FDA, sometime in "the late 1970s it became increasingly clear that many citizens were being left out of … [ongoing medical and scientific] advances. One of the key reasons for this neglect was the small size of some patient populations. The relatively limited prevalence of a particular disease acted as a barrier for commercial investment in the research and development required to show evidence of the safety and efficacy of treatments. Ironically, by the early 1980s, these "rare diseases" affected 20-25 million patients who, together, suffered from approximately 5000 rare diseases…" Regarding rare and orphan diseases:

- There are approximately 7,000-10,000 known rare diseases
- Aggregate U.S. patient population estimated at about 25-30 million
- Generally, they tend to be chronic, serious and frequently life-threatening
- Majority (about 80%) are genetic in origin
- More than 90% have no FDA-approved treatment

Source: NIH, NORD, Company reports

The Office of Orphan Products Development was created to encourage development of products to treat orphan diseases. The Orphan Drug Act was designed to stimulate innovation regarding treatment for rare and orphan diseases. The Orphan Drug Act of 1983 created financial incentives to develop therapies, including a seven-year exclusive period to market a drug approved to treat an orphan disease, even if it was not under patent, and tax credits for R&D and other expenses. The FDA notes that by 1990, it "had designated 370 products for orphan status, and of these 49 were approved for orphan indications. By 2002 the number of orphan designations grew to almost 1100, and approvals to 232, a number that provided treatment to an estimated 11 million patients."

Significantly Higher Cost of Orphan Drugs

The number of diseases designated as orphan diseases has increased geometrically and the number of drugs to treat many of those disorders has also increased as the FDA has sought to accelerate their approval. This gives us confidence of the company's ability to move QRX003 through the approval process domestically and internationally, given the need for novel treatment therapies for the diseases for which it is developing QRX003.

Costs of these treatments generally are significantly higher than costs of treatments for wider spread disorders. According to a study conducted by the National Institute of Health (NIH), "the cost per patient per year for a patient with a rare disease ranged from $8,812 to $140,044, compared to $5,862 for those without a rare disease." This estimate takes into account annual direct medical costs and indirect costs. The estimated direct costs of treating all patients afflicted with a rare or orphan disorder, including drug costs, hospitalizations and other expenses, aggregates to an estimated roughly $400 billion, which is comparable to major diseases such as cancer, heart failure or Alzheimer's.

Other estimates are in-line with NIH's. The United States Government Accountability Office (GAO) found that the "total cost in the United States for the estimated 15.5 million people with these 379 rare diseases was $966 billion. This amount reflects the combination of direct medical costs (estimated about $418 billion) and indirect costs associated with productivity losses ($437 billion), plus direct nonmedical costs. The company cites estimates that orphan drug sales could reach $242 billion by 2024. In the aggregate, the market sizes and commercial opportunities of treatments that Quoin's products address could represent a sizable market if Quoin can commercialize its product portfolio in an efficient way, as management expects, and address multiple indications with most products. By developing and then launching products centered around dermatological disorders, with treatments that can effectively treat multiple disorders, the company expects to obtain economies of scale on development, distribution and go-to-market costs.

Competition

Several other companies are also developing treatments for NS. As noted, however, the company believes it is the only pharmaceutical company conducting dual clinical NS trials under an open IND application. Krystal Biotech, for example, has KB104 under development for the treatment of Netherton Syndrome. KB104 is a topical gel formulation designed to deliver two copies of the SPINK5 transgene. BridgeBio Pharma is developing BBP-561, a topical treatment therapy. Novartis had conducted clinical trials for BPR277, a topical treatment for atopic dermatitis and NS, and subsequently licensed the treatment to San Francisco-based LifeMax Laboratories.

In 2020, Toronto Innovation Acceleration Partners (TIAP) and others invested in a drug development project focused on NS. Separately, privately-held Azitra received Rare Pediatric Disease Designation for ATR-12 for the treatment of Netherton syndrome. We would expect multiple products could achieve market if their clinical trials produce effective therapies.

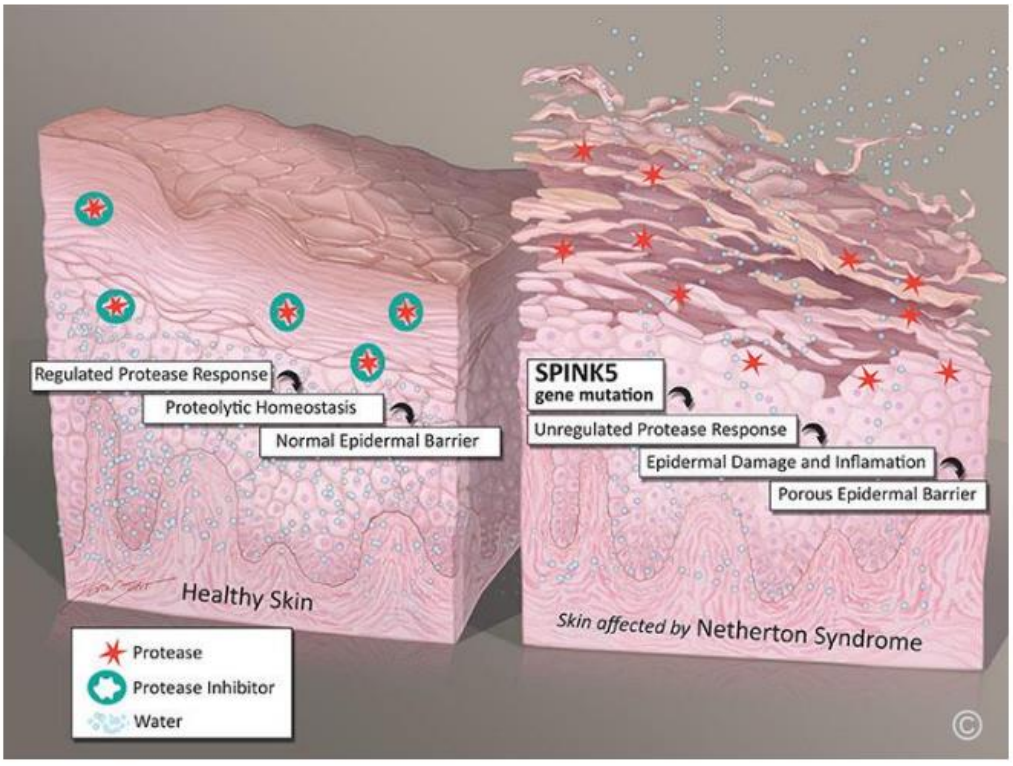
Netherton Syndrome

Netherton Syndrome is a debilitating skin disorder caused by mutations in the Serine Protease Inhibitor Kazal-type 5 (SPINK5) gene, SPINK5 is crucial in regulating serine proteases that hydrolyze extracellular proteins that bind corneocytes. In other words, SPINK5 is critical to the skin's regular and necessary shedding and replenishing and moisture retention.

People suffering from Netherton syndrome do not have as many layers of outer skin (stratum corneum) as they need, which means that their skin does not perform its primary function as a protective barrier. In turn, this increases the risk of infections, warts, irritation and even skin cancer in some patients. Moreover, their skin tends to be prone to scaling and is accompanied by hair anomalies, along with increased susceptibility to atopic eczema and itching. Patients with NS can also experience trans-epidermal water loss (TEWL).

Patients can suffer with painful symptoms such as predisposition to allergies, asthma, and eczema, congenital ichthyosiform erythroderma, hair shaft defects and recurring infections, chronic skin inflammation, severe dehydration, and stunted growth, among others. Babies who are born with NS tend to develop slower than others and often gain weight slowly, as well, which can put them at high risk of infection and dehydration. In turn, this can be severe and ultimately life threatening. Severe NS In infants can be associated with failure to thrive, delayed growth, short stature, and recurrent infections. According to the NIH, NS symptoms – including red, scaly skin – generally present at birth. Symptoms could include outbreaks of red, circular scaly rashes, and as noted, thin, fragile hair (bamboo hair), and immune reactions such as hay fever, asthma, itchy skin, and eczema.

Netherton Syndrome



Source and copyright: Quoin Pharma

The NIH notes that "[t]here is no specific treatment" for Netherton syndrome. Current standard of care seeks to manage the associated symptoms and complications. Standard therapies currently include regular use of lotions and emollients. However, because the patient's skin protective barrier is compromised, certain topical ingredients could cause adverse reactions. Because skin inflammation/infection/allergy and skin barrier defect are mutually causal, using one therapeutic strategy generally is not an optimal solution.

Epidermolysis Bullosa

Epidermolysis Bullosa (EB) is a group of rare and genetic skin disorders. A person with EB generally has skin that is so fragile that even minor trauma can result in serious and severe pain, or even blistering, scarring, infections, chronic wounds. If severe enough, the disease could ultimately lead to the patient's immobility, disfigurement, disability and even early death. Recessive Dystrophic (RDEB), a form of EB, is characterized by progressive and increasingly painful blistering. It is diagnosed at infancy and results in a high mortality rate. Some 76% of patients diagnosed with RDEB do not reach the age of about 40. There is no cure or approved treatments.

Peeling Skin Syndrome

The NIH defines Peeling skin syndrome (PSS) **as** "a group of conditions that causes skin to peel and tear easily" and is caused by genetic variants in several genes. In some people with PSS, the skin peeling is limited to the hands and feet. In addition to continuous peeling of the skin, some people who suffer with PSS experience itching, redness, and scarring. Symptoms generally occur by childhood, but can appear anytime from birth to adulthood.

Palmoplantar Keratoderma

The NIH defines Palmoplantar keratoderma (PPK) as "a group of skin conditions characterized by thickening of the skin on the palms of the hands and soles of the feet." In some rare cases, PPK can also affect organs other than the skin.

Scleroderma

According to the Scleroderma Research Foundation (SRF), Scleroderma is an autoimmune disorder that causes inflammation in the skin and other areas of the body. The inflammation triggers the immune system to over-produce collagen, which in turn leads to the hardening and tightening of the skin and connective tissues (ie: fibrosis). In the most serious cases, there can be complications resulting in damage to the heart, lungs, and digestive system. Scleroderma is "a complex disease that can progress in very variable ways in individual patients," according to SRF, which frequently makes it difficult to diagnose.

RECENT RESULTS

Quoin registered 2Q24 OpEx of $2.1 million, down from $2.3 million in 2Q23. G&A expenses of about $1.6 million were about 1% lower, primarily due to a shift in allocation of expense. QNRX reported a net loss just shy of $2.0 million, or ($0.39) per share on about 5.0 million ADSs outstanding (FD) compared to a net loss of $2.1 million or ($2.13) per share in 2Q23 on about 1.0 million ADSs.

At the end of 2Q24, QNRX had about $12.6 million in cash and equivalents. Quoin completed a capital raise earlier this year to strengthen its financial position and ability to continue to move QRX003 and other candidates forward. In addition, QNRX entered into an arrangement with Alumni Capital LP for an equity line of credit for up to $8 million. Management believes that through these measures, it has extended its cash to maintain activities into late 2025.

VALUATION

General market volatility, the uncertain economic and interest rate outlook, further potential dilution and uncertainty over if/whether QRX003 and other assets will attain regulatory approval are factors that overhang QNRX shares, in our view, just as these factors hurt many emerging microcap companies. Nevertheless, we remain optimistic about the chances of QRX003 receiving FDA and other approvals and the subsequent commercial demand, beginning with as NS treatment and potentially for multiple indications. The absence of alternative effective therapies that have the limited side effects, combined with relatively high related healthcare costs of the target patient populations could translate, we believe, into solid demand for QRX003 following clinical studies of its efficacy for a range of indications. Given the early stage of the company's development and the uncertain economic outlook, we assign a 40%-50% confidence multiple to our revenue forecast range at this point. However, depending on clinical efforts, regulatory approval and commercial launches, our confidence multiple might prove conservative. Thus, we might increase / lower our confidence multiple in the future.

Quoin estimates the NS patient population in the U.S. and EU at about 6,000 to 7,000. It is not difficult to see how revenue for QRX003 could build, depending on the market share the product captures, annual treatment cost and Quoin's retention after revenue sharing with distribution partners and/ or sales commissions. The scenarios presented below represent the potential commercial opportunity for QRX003 for NS alone. Aggregate demand from patients suffering with peeling skin disease and potentially other indications could translate into revenue upside, in our view.

It is difficult to know the revenue arc for QRX003 at this early stage. Nevertheless, we believe it is reasonable to expect that Quoin could attain product revenue of $14 million to $20 million by 2027-28, depending on when / if QRX003 obtains regulatory approval and other factors noted above. We base this range on the company's expected launch timeline and depending on factors noted above, patient population, potential for QRX003 to achieve 15% or greater market share and expected treatment costs. Quoin believes QRX003 represents a strong treatment option. Moreover, it would seem likely that the market can support multiple products, in our view.

Applying a 1.4x to 2x multiple (based on other clinical stage companies, low to mid end of the range) to the above noted possible revenue range and discounting back to the present at 11%/year results in a present value of roughly $14 million to $20 million. Applying a confidence multiple at the lower end of the range on potential timeline delays yields a mean valuation of about $2.00 per ADS. We believe the ADSs can attain this valuation as the company hits certain milestones, although we do not expect the shares to mirror this potential until further advances are made. We also believe current general market conditions, the uncertain economic outlook and risk of Nasdaq delisting – QNRX was notified by Nasdaq that its shares were not in compliance with minimum price of $1.00 and has until October 28, 2024, to regain compliance -- could continue to overhang the shares.

Any delay or failure in clinical development or regulatory approval could cause the share price to decline and represent a potential risk to our valuation but we believe the risk / reward ratio could be attractive for investors who have a higher than average risk tolerance and longer time horizon.

RISKS

Risks to Quoin achieving its objectives, and to our valuation, include the following, among others.

- Quoin might need to raise additional capital earlier than expected.
- Clinical and commercialization timelines could be delayed by factors outside Quoin's control.
- The company might not gain traction as quickly as it expects if/when it commercializes its assets.
- Clinical results might not meet the company's expectations.
- The company might not obtain regulatory approvals in the time expected or at all.
- Competition for QRX003 and other assets could be steeper than anticipated and could also increase.
- Quoin faces going concern risks.
- Quoin shares risk not meeting Nasdaq listing compliance.

RECENT NEWS

- Quoin announced 2Q24 results and provided a corporate update on August 8, 2024.
- On August 6, 2024, Quoin announced plans to initiate a clinical study for Peeling Skin Syndrome.
- QNRX announced international expansion of its ongoing clinical trials for NS on June 27, 2024.
- The company signed a research agreement with University College Cork (UCC) on June 12, 2024.
- Quoin announced the pricing of its $6.5 million offering on March 5, 2024.
- Quoin announced receipt of FDA clearance to recruit teen subjects into both ongoing NS clinical studies on March 4, 2024.
- On February 8, 2024, Quoin filed U.S. and international patent applications for novel NS combination product.
- Quoin announced 3Q23 results & provided a corporate update on November 8, 2023.
- On October 24, 2023, Quoin announced additional positive clinical data from its open-label trial in Netherton Syndrome.
- On July 17, 2023, Quoin announced the change in the ratio of its ADSs from 5,000 ordinary shares to one ADS representing 60,000 ordinary shares, with no change to the ordinary shares.

PROJECTED FINANCIALS

Quoin Pharmaceutical Income Statement & Projections (US $000 except per share data

	2022	1Q23	2Q23A	3Q23A	4Q23	2023A	1Q24A	2Q24A	3Q24E	4Q24E	2024E
Revenue	-	-	-	-	-	-	-		-	-	-
Operating expenses											
General and administrative	6,584.9	1,683.8	1,635.0	1,366.5	1,385.3	6,070.5	1,615.5	1,617.8			
Research and development	2,672.8	1,091.7	625.1	758.8	832.4	3,308.0	842.8	519.3	-	-	-
Total operating expenses	9,257.7	2,775.6	2,260.1	2,125.2	2,217.7	9,378.5	2,458.3	2,137.1	2,386.6	2,361.1	9,343.1
Operating loss	(9,257.7)	(2,775.6)	(2,260.1)	(2,125.2)	(2,217.7)	(9,378.5)	(2,458.3)	(2,137.1)	(2,386.6)	(2,361.1)	(9,343.1)
Other											
Forgiveness of accounts payable	(416.0)	-	-		-						
Warrant liability (income) expense	(77.2)	-	-		-						
Unrealized loss / inc	(1.3)	(20.4)	-		23.1	2.7	6.5	2.2			
Interest income	(95.7)	(152.1)	34.5	(2.1)	(574.9)	(694.6)	(137.5)	(165.3)			
Other	714.1	-	(187.6)	(196.4)	384.0	-	-	-	-	-	-
Total other income	123.8	(172.5)	(153.1)	(198.5)	(167.8)	(691.9)	(131.0)	(163.1)	(109.2)	(110.3)	(513.6)
Net loss	(9,381.5)	(2,603.1)	(2,106.9)	(1,926.7)	(2,049.9)	(8,686.6)	(2,327.3)	(1,974.0)	(2,277.4)	(2,250.8)	(8,829.5)
Dividend on warrant modification	(65.3)										
Net loss to shareholders	(9,446.8)	(2,603.1)	(2,106.9)	(1,926.7)	(2,049.9)	(8,686.6)	(2,327.3)	(1,974.0)	(2,277.4)	(2,250.8)	(8,829.5)
Loss per ADS*	($3.90)	($4.09)	($2.13)	($1.95)	($2.08)	($9.64)	($1.11)	($0.39)	($0.44)	($0.44)	($2.02)
Weighted avg ADSs outstanding	2,421.9	637.2	987.2	987.2	987.2	900.9	2,103.3	5,049.7	5,149.7	5,150.7	4,363.4

Source: Company reports & Zacks One ADS = 1 ordinary share as of 11/23 *ADS ratio PF

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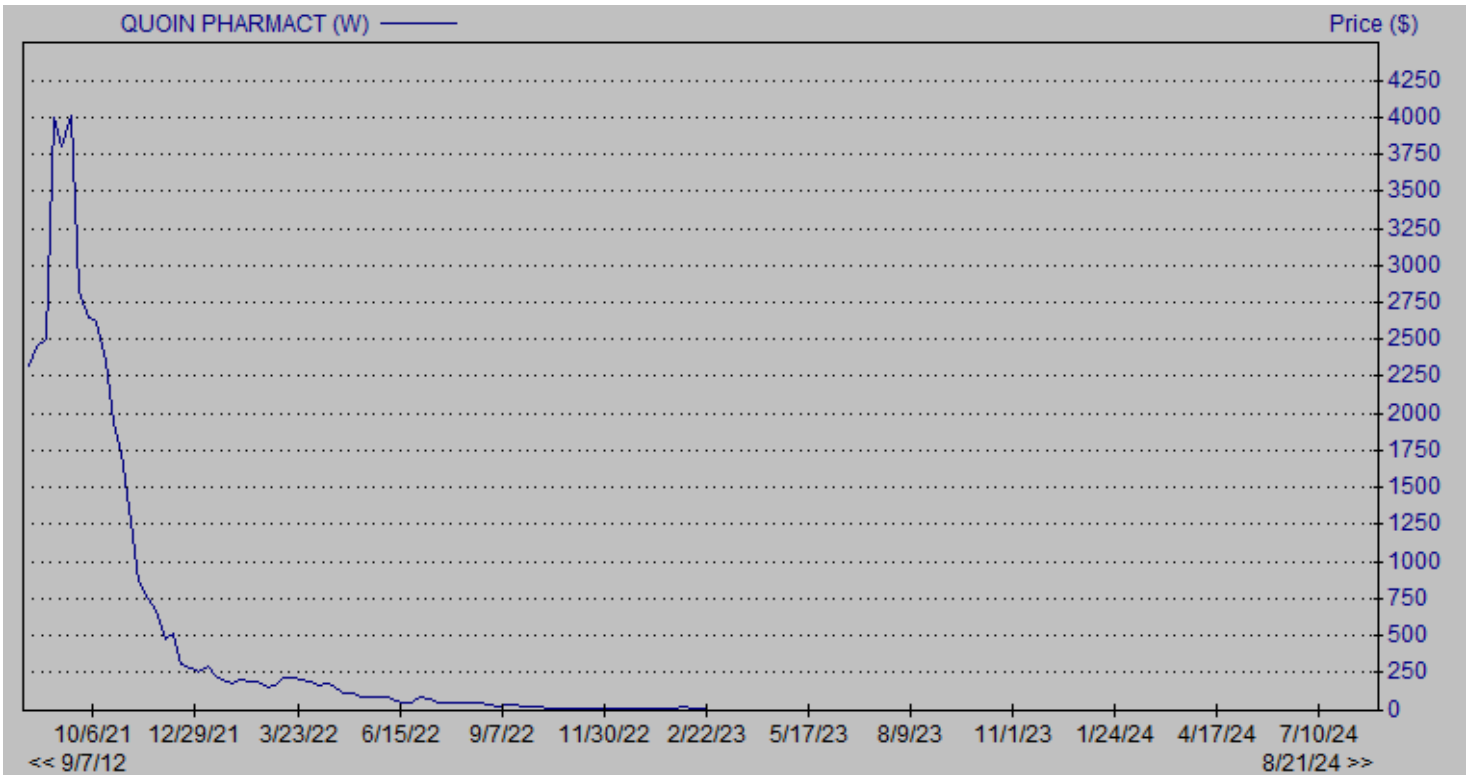
HISTORICAL STOCK PRICE



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