NUFORMIX PLC

Optimising therapies and unlocking value

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Nuformix Plc - Key data	
Code	NFX.L
Listing	STANDARD LIST
Shares in issue (m)	591.609
Share price (p)	2.4
Market Cap (£m)	£14.2
52 week Max (p)	6.60
52 week Min (p)	2.35
Sector	Healthcare

Source: Company data, Reuters Eikon. (Shares post financing).

SHARE PRICE PERFORMANCE

Source: Reuters Eikon

INVESTMENT OVERVIEW

Nuformix (NFX) is a pharmaceutical development company, targeting unmet medical needs in fibrosis and oncology via drug repurposing: it uses its expertise in discovering, developing and patenting novel drug forms, with improved physical properties, to develop new products in new indications that are, importantly, differentiated from the original (by way of dosage, delivery route or presentation), thus bringing new and attractive commercial opportunities. NFX's early-stage pipeline has potential for significant value and early licensing opportunities. NFX's business model is to take its assets to key value creation inflection points before partnering or licensing.

Optimising therapies and unlocking value

NFX uses its expertise in solid form science to discover and file patent applications on new solid forms to facilitate development of alternative formulations and delivery methods to repurpose known drugs into differentiated medicines for new indications. The commercial value potential of NFX's repurposed product concepts is maximised through differentiation from the original product, patent protection and development for new indications where there is a strong scientific rationale. Lead programme is NXP002, being developed as an inhaled drug to address unmet needs in Idiopathic Pulmonary Fibrosis (IPF), a devastating and deadly disease, with a significant commercial opportunity.

NXP002 - for the treatment of a devastating lung disease

NFX's lead asset is NXP002, which is a new form of the drug tranilast, in an inhaled formulation, being developed for the treatment of IPF, which is a devastating lung disease associated with a higher mortality than many cancers and where the need for additional treatment options is acute. Tranilast has a long history of safe use as an oral drug for allergies but with evidence that supports its potential in fibrosis, including IPF. Recent market precedent shows IPF remains an area of huge interest to big pharma, even at an early stage: AstraZeneca recently licensed Redx Pharma (REDX)'s preclinical IPF programme for a package worth $377m, plus royalties.

Expertise in repurposing allows NFX to maximise commercial opportunities

Repurposing is a well-known strategy for leveraging the therapeutic and commercial value of established drugs. NFX uses its expertise in solid form science to discover and file patent applications on new solid forms to facilitate development of alternative formulations and delivery methods to repurpose known drugs into new indications. NFX sees a clear opportunity to extract value from its pipeline of assets for fibrosis and oncology, that are therapy areas with high unmet medical needs and offer significant commercial potential. Repurposing clearly can bring benefits to patients through new treatments, but crucially, a repurposing programme can be completed in less than 10 years, with much higher probability of success, and at c 10% of the costs of developing a new drug. The success of repurposing is readily exemplified by Biogen's oral Multiple Sclerosis treatment Tecfidera®, which delivered > $4bn sales in 2019. Here the original product (a psoriasis cream) was repurposed into an orally delivered product, enabling development for the new indication and re-launching its therapeutic and commercial scope.

Taking assets to key value inflection points before partnering or licensing

NFX has an early-stage pipeline of preclinical and Phase 1-ready assets with potential for significant value and early licensing opportunities. The business model is to take its assets to key value inflection points before partnering or licensing. The pipeline comprises: 1) lead program NXP002 (inhaled tranilast) in the preclinical stage, 2) Phase I ready programme NXP001 (aprepitant) in oncology, where a decision by private company, Oxilio, to exercise its exclusive option to agree a global license is imminent and will determine the way forward and 3) NXP004 (drug not disclosed), a preclinical stage programme, based on a blockbuster cancer drug (sales >$1bn) where, pending additional research data and patent filings, the priority is to offer an improved form of the original drug in oncology.

Key shareholders

Shareholder	Holding
CPI Enterprises	7.7%
Dr D J Gooding	7.3%
Dr J M Holland	7.3%
Alan Chorlton	4.7%
Mr J Higgins	4.0%
Dave Tapolczay	3.5%

Source: Company data (holdings pre financing)

NXP002 – formulated as an inhaled product

NXP002 is differentiated from the original drug as it is being formulated as an inhaled product delivering drug direct to the lung, which is a well-known strategy for treatment of lung diseases to yield greater efficacy and reduce systemic side-effects compared to oral treatment. Marketed precedent for inhaled products shows efficacy can be achieved at doses less than a tenth of that for an oral drug.

NFX expertise in inhaled therapies progressing NXP002 to next inflection point

In addition to literature data on tranilast in fibrosis, NFX has generated its own promising, but early, data to show that NXP002 performs better than IPF standard of care in preclinical models, notably in lung slices taken from IPF lung transplant patients. NFX will apply its extensive expertise in inhaled therapies to advance the programme to the next inflection point in six-to nine months' time and, if the planned preclinical studies support its earlier promise, seek licensing partners thereafter. We calculate global peak sales of £1bn for this asset in IPF. **NFX has raised £1.565m gross (£1.4m net) issuing 78,250,000 new shares, to progress its near-term strategy including to support the development of a preclinical data package for lead asset NXP002 for IPF.**

NFX DCF valuation of 9p per share post funding

Our DCF valuation of NFX includes only NXP002 at this stage. Using a 13% WACC gives a risk adjusted valuation of £52.8m, equivalent to 9 pence per share, and this assumes that a Phase I ready package for NXP002 is in place. Subject to financing, NFX anticipates that this milestone could be achieved within the next 18 months, but with multiple opportunities for licensing NXP002 prior to this. Prospects for an early-stage deal are good judging by precedent in the IPF space.

COMPANY HISTORY

Nuformix (NFX) listed on the London Stock Exchange Main Market (Standard List) in October 2017 via a reverse takeover into Levrett plc, at a valuation of £12m, raising £2.3m in parallel. It was founded in 2008 based on its core expertise of discovering and characterising novel physical forms.

The recent appointment of Dr Anne Brindley as CEO brings a wealth of leadership expertise in large pharma and smaller companies including product development as well as business development/licensing and M&A experience, having sold the last company she worked for, and she has a broad network of contacts. Her expertise is focussed on small molecules for respiratory and oncology indications and she specialises in inhaled therapies, from development to market approval, complementing existing expertise within NFX.

Company Strategy and Business Model

NFX is targeting unmet medical needs in fibrosis and oncology via drug repurposing: it uses its expertise in discovering, developing and patenting novel drug forms, with improved physical properties, to develop new products in new indications, that are, importantly, differentiated from the original (e.g. by way of dosage, delivery route or presentation), thus bringing new and attractive commercial opportunities.

NFX is specialising in fibrosis and oncology although its technology can be universally applied to any molecule and indication. The lead programme is NXP002, being developed as an inhaled drug to address unmet needs in Idiopathic Pulmonary Fibrosis (IPF) a disease with high mortality rate and with few approved treatment options.

The Company's current business model is to take its early stage pipeline assets to key value inflection points before partnering or licensing. To achieve this the company is seeking to optimise the value from existing assets by prioritising the lead asset NXP002 and performing further preclinical studies to generate a more robust data package to increase the value for this asset, thereby making it more attracting to licensing partners. The Company operates a very lean, fully virtual, operating model, outsourcing to CROs or to partners, to minimise its cost base.

DRUG REPURPOSING UNLOCKS THERAPEUTIC AND COMMERCIAL SCOPE

NFX is targeting fibrosis and oncology via drug repurposing. For NFX, repurposing involves not only developing the known drug in a new indication but differentiating it from the original product via discovering new physical forms of the drug that allow the drug to be delivered by a new route or a new formulation. Drug repurposing is a major strategy for revitalising older drugs, or finding new ways to treat different diseases more effectively: an estimated 30%[1] of all FDA drugs approved are repurposed. The COVID-19 pandemic has provided an all too clear illustration of the therapeutic value and accelerated route to market via drug repurposing strategy. Gilead's anti-viral Veklury/remdesivir received EUA for treating severe COVID in 2020, but was originally launched for Hepatitis-C and RSV back in 2014, while the corticosteroid dexamethasone, a mainstay of rheumatic disease treatment. was endorsed by EMA in September for COVID patients requiring oxygen therapy.

In addition to the potential therapeutic benefits, drug repurposing can reduce the risk and cost versus developing a drug from scratch, via abbreviated regulatory pathways, by leveraging existing Pharmacokinetics (PK) and safety data. There is also good precedent for market success for differentiated repurposed drugs illustrating that this strategy route is highly commercially attractive.

Repurposing existing drugs into new indications using novel forms, that enable new formulations to be developed, importantly differentiates the product, by virtue of the alternative formulation and/or route of administration, bringing commercial value. By developing robust IP for these novel drug forms, with patent protection of up to 20 years (essentially the same as for a new chemical entity), this enables attractive commercial returns to be generated and prevents generic competition. New forms and formulations may also be developed to extend the life cycle of generic drugs, in parallel with targeting a new indication and improving therapeutic benefits and/or the mode of administration and this one of the potential options to explore for NXP004.

In summary these repurposing benefits include:

- Development of known drugs in new indications and formulations, differentiating from the original drug and adding commercial value
- Improvement in the physical properties and adjustment of the mode of administration which can provide a significant differentiation and enhance therapeutic value.
- Up to a 20% reduction in risk, development timelines and only a fraction of the cost of development compared to the traditional model.
- Extension of the life cycle of a generic drug for example, helping to avoid losing revenues from off patent blockbuster drugs.

Notable repurposing successes include the topical psoriasis cream Fumaderm (active ingredient: dimethyl fumarate), originally developed by Fumapharm, which was acquired by Biogen who then repurposed this as an **oral Multiple Sclerosis treatment called Tecfidera®, which delivered over $4bn in 2019 revenues**.

NFX is applying its know-how in discovering and developing new small molecule drug forms and formulations to open up the broad therapeutic potential of existing drugs

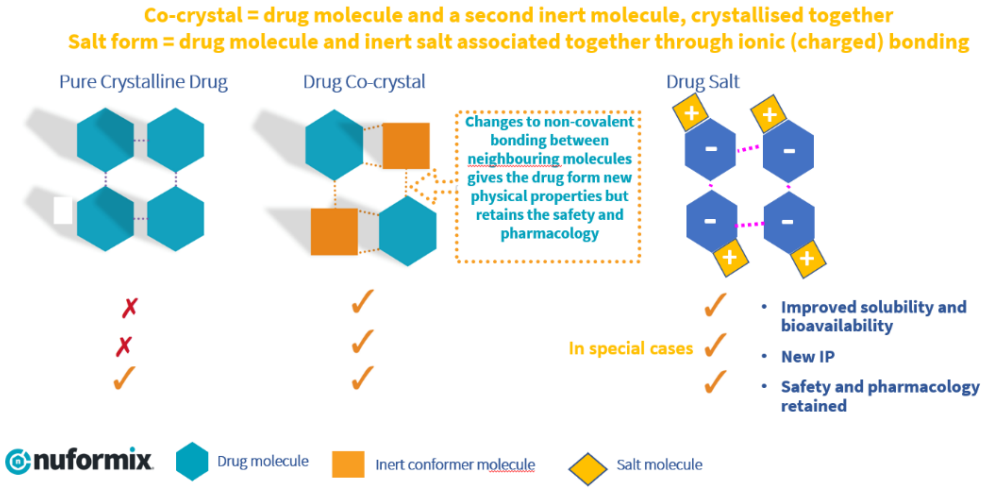
[1] Cha Y, et al. Drug repurposing from the perspective of pharmaceutical companies. British Journal of Pharmacology. 2018

where there is a strong commercial rationale and where there are particular therapeutic benefits to be gained.

Such solid form techniques can improve the solubility and bioavailability of drugs, removing the barriers to reformulation, improving their physical and therapeutic features. While many drugs have multiple mechanisms suited to new disease areas, it is estimated that 40% of existing drug products have limited solubility and therefore cannot be delivered to the body effectively. NFX focuses on leveraging expertise in well embedded solid form techniques to create new chemical forms of old drugs, primarily:

- Drug co-crystals: drug molecule and a second molecule, crystallised together through non-covalent interactions.
- Drug salts: drug molecule and a second molecule associated together through ionic (charged) bonding.

PHARMACEUTICAL PROPERTIES AND BENEFITS OF CO-CRYSTALS AND SALT FORMS



Source: Nuformix

The structure of a crystalline drug directly affects its solubility in solution which impacts on bioavailability and ability to exert its positive effects on the body. This presents a major challenge- **if a drug cannot dissolve in the gastrointestinal tract or penetrate the tissues, its therapeutic applications are limited.**

Creating new drug forms can also improve:

- Purity
- Stability
- Ability to formulate and manufacture
- Thermal and physical properties of the drug under changed conditions.

DELIVERY KEY TO DRUG DIFFERENTATION AND OPTIMISATION

Another important feature of NFX's strategy is that the solid form techniques it uses are capable of adapting a drug to any route of administration, so it has expertise to create differentiated drugs, via a lower risk model, which might be better suited to a particular disease setting than the original drug.

- New solid forms are suitable for oral, injectable, inhaled, ophthalmic, topical routes - this can transform the therapeutic options, improve bioavailability which we discuss in greater depth below. New CEO Dr Anne Brindley has particular expertise in formulation, clinical development and commercialisation of inhaled therapies notably flutiform® (Vectura/Mundipharma/Kyorin) and Symbicort® (AstraZeneca) which are core inhaled products in the multi-billion dollar asthma and COPD market.

- New delivery route can be better suited to the indication to enable a differentiated, patentable product.

- Provides attractive potential to create an optimised drug form.

Regulatory change unleashes new commercial opportunity

There is well-documented evidence on the many different benefits of pharmaceutical co-crystals and salts and other key solid form techniques. Regulatory change dating from 2016 caused a major shift in the classification of co-crystals, underlining the commercial rationale.

The specific regulatory factors surrounding co-crystals mean that they are treated as exactly equivalent to the parent drug. This is a highly significant factor since it removes the need to repeat toxicology and safety studies and hence co-crystals can be developed via accelerated pathways. A key concept in the utilisation of co-crystals is that there is no change in the chemical structure of the drug.

The FDA modified their guidance in February 2016 which was finalised in 2018. This draft guidance classified co-crystals as active pharmaceutical ingredients (APIs), not drug product intermediates, and endorsed co-crystals as equivalent to polymorphs of the API.

This significant development enables both proprietary and generic companies to access the abbreviated ANDA and 505(b)(2) development pathways for drug approval in the USA and Europe.

A novel API or biologic typically takes 10–15 years to go from initial idea to marketing approval with an attrition rate of over 80%, while a repurposing or repositioning programme can commonly be completed in less than 10 years and with much higher probability of success.

COMMERCIAL PRECEDENT

Around 30% of all FDA drug approvals are repurposed drugs, and a similar proportion of revenues[2] according to some sources, indicating the enormous interest and commercial prospects. A selection of examples showing buoyant licensing and M&A activity is shown below.

DRUG REPURPOSING DEALS

Company	Drug	Repurposed indication	Original indication	Product change from original	Acquirer/Licensor (Year)	Status at time of deal	Deal Value (USD)
Vicept Therapeutics	Rhofade (oxymetazoline)	Rosacea (topical cream)	Decongestant (nasal spray)	New indication + route	Allergan (2011)	Phase II complete	200m (acquisition)
Arakis (Sosei)/Vectura	Seebri/Ultibro (glycopyrronium)	COPD (inhaled)	Ulcers/Excessive sweating (Oral/IV)	New indication + route	Novartis (2005)	Phase II	375m
Aspreva Pharma	Cellcept (mycophenolate)	Lupus nephritis (oral)	Immunosuppressant (oral)	New indication	Galenica Holdings (2008)	Phase III ongoing	915m (acquisition)
Ceptaris Therapeutics	Valchlor (mechloroethamine)	Lymphoma (oral)	Mustard gas (chemical warfare)	New indication + formulation	Actelion (2013)	On approval	250m (acquisition)
Esteve	celecoxib+tramadol combination	Severe acute pain	Individually marketed for mild to moderate pain	New indication + new cocrystal form	Mundipharma (2015)	Phase 2 complete	>1 billion (second asset included)
New River	Vyvanse (lisdexamfetamine dimesylate)	ADHD	Originally marketed as mix of 4 amphetamine salts (Adderall)	New prodrug form	Shire (2007)	Phase III ongoing	2.6 billion (acquisition)
Medivation	Dimebon (latepiridine)	Alzheimers	Antihistamine (Russia only)	New indication, new geography	Pfizer (2008)	Phase II	725m
Nektar Therapeutics	Movantik (PEGylated naloxol)	Opioid induced constipation	IV for opioid overdose (as parent drug naloxone)	Pegylated form of drug	AstraZeneca (2009)	Phase II complete	735m
Novartis	TOBI Podhaler and liquid (tobramycin)	Cystic Fibrosis (inhaled)	Antibiotic (IV)	New indication + route	Mylan (2018)	Marketed	463m

Source: Nuformix and Company data

Utilisation of co-crystal technology itself is widely documented in association with well-known drugs like aspirin and ibuprofen, to improve characteristics such as solubility, stability and absorption, modifying physicochemical properties, without altering the pharmacological characteristics of drugs.

A more recent success in the class, which overcome stability, reproducibility and quality challenges via a co-crystal formulation is Merck/Pfizer's SGLT2 inhibitor Steglatro (Ipragliflozin) (estimated peak sales over $1bn) the co-crystal was developed in order to improve drug quality[3], since ipragliflozin was unstable depending on changes in heat and moisture (hygrothermal conditions).

[2] IBID

[3] Cocrystal of C-glycoside derivative and L-proline - Patent US8097592B2. 2007.

Deal precedent illustrating the attractions of repurposing using co-crystals includes Mundipharma's 2015 co-development deal with Esteve, worth up to $1bn, to access its then Phase II asset tramadol celecoxib co-crystal (E-58425) for post-operative pain, currently in Phase III studies. The use of co-crystal technology was effectively used to couple two API's together and create a novel product.

OPTIMISATION AND A GLOBAL STRATEGY

NFX focuses on repurposing and reformulating small molecule drugs where there is a significant commercial and clinical value. In all cases, NFX seeks to maximise value by signing early global licensing deals where possible, to share in commercial returns. This includes:

- Licensing its internal pipeline after the preclinical package or robust IP has been developed.
- Licensing its know-how and IP to advance new forms of third party candidates for novel indications or to extend life cycle of the drug.

The Company has a broad published patent portfolio with mostly granted patents, covering novel physical forms of five drugs with other applications pending. There are three programmes in the focused pipeline. Its lead internal programme is NXP002, an inhaled treatment for Idiopathic Pulmonary Fibrosis (IPF). It is based on the parent drug, tranilast which was first approved to treat allergies and bronchial asthma, and which has a long history of safe use.

NUFORMIX PORTFOLIO AND PIPELINE

Programme	Lead Indication	Status	Notes
NXP002 (tranilast)	Inhaled therapy for Fibrotic disease initially IPF as monotherapy or in combination with SoC	Preclinical	Lead programme, next step; generate further preclinical data progressing towards Phase I ready package, seek licensing opportunities.
NXP001 (aprepitant)	Oncology unspecified	Phase I-ready	Option agreement with Oxilio expires 24 March 2021; agree licensing deal or seek other licensing opportunities in cancer
NXP004 (undisclosed)	Oncology	Preclinical	One patent application filed. Potential to augment IP and license

Source: Nuformix

NFX is repurposing tranilast since there is well documented, scientific preclinical evidence of its multiple mechanisms carried out independently. Numerous studies show its activity in models of fibrosis including IPF. NFX seeks to unlock its therapeutic potential in IPF, in which there are just two therapies approved. There is a clear opportunity to enhance and build upon the limited treatment options, to leverage tranilast and to reformat the drug for inhaled delivery to provide significant differentiation. NFX has developed promising but early data to show that NXP002 performs better than standard of care in preclinical models, and is applying its expertise in solid forms and inhaled therapy to advance the programme to the next inflection point.

Oncology programme NXP001(new form of aprepitant) is being evaluated initially via NFX's strategic alliance with Oxilio, pending an outcome decision regarding the latter's option to advance, due by 24 March, which will determine the next steps and a potential licensing agreement. If the option is not exercised, Nuformix will evaluate additional business development opportunities for NXP001 in oncology.

NXP004 is a new physical form of an undisclosed oncology drug. It is being evaluated to assess its scope and the commercial options include the lifecycle extension of this blockbuster drug and its return to the originator via reformulation, or alternatively licensing to a generic pharma company. There is literature data on this drug in fibrosis and NFX has performed some studies in this area, however, to derive most value from this asset, the focus of the company for NXP004 is oncology.

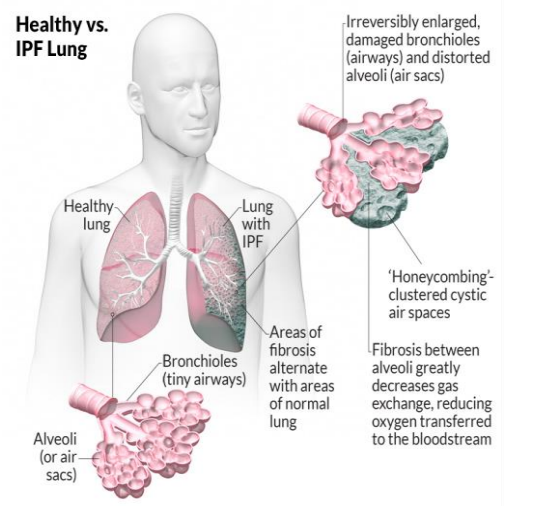
NFX is seeking to maximise the clinical and commercial scope of all its pipeline. Its priority is NXP002, where there are exciting prospects for an inhaled form offering a site-targeted approach in IPF, a market opportunity with an estimated value of $3bn and set to rise to over $4bn this decade.

AN INNOVATIVE APPROACH TO TREATING IPF

Idiopathic pulmonary fibrosis (IPF) is an aggressive, incurable lung disease characterised by a loss of lung function, inflammation and with an average survival rate of just three to five years from diagnosis, worse than many of the common forms of cancer such as breast cancer, colon cancer and leukaemia. Patients suffer damage and scarring of the lungs leading to a severe decline in function, breathlessness, and debilitation requiring oxygen supplementation followed by respiratory failure and death.

IPF affects approx. 160,000 people in the top 5 European nations, and around 140,000 in US with an annual incidence of new cases of 1-2%. The underlying cause of IPF is unknown although it is thought that certain environmental triggers in combination with genetics, are at play. It is a challenging disease to treat, owing to its multiple mechanisms and complications, and is characterised by periods of slower progression followed by acute exacerbation. Breathlessness and cough are the most common symptoms which severely impede quality of life of IPF sufferers. Diagnosis is usually made via computed tomography (CT), bronchoscopy, breathing test or biopsy although accurate evaluation of disease severity and prediction of disease progression is challenging and limited by the lack of standardised measures.

LUNG SCARRING IN IPF



Source: Nuformix

Treatment options focus on slowing the formation of scar tissue and controlling symptoms. Lung function test values such as forced vital capacity (FVC) a measurement of the ability to inhale and exhale is the most commonly used lung function parameter for measuring IPF severity, progression and response to treatment. An absolute decline in FVC of ≥10% over 6 months is regarded as clinically important and is frequently used to describe 'significant' disease progression.

AN AGGRESSIVE DISEASE WITH LIMITED TREATMENT OPTIONS

There are only two approved pharmacological treatments for IPF, both of which are oral treatments which delay disease progression, and respiratory failure, rather than providing a cure for the disease. Yet they still have combined annual sales of around $3bn. Roche's 2014 takeover of US biotech InterMune for $8.3bn was motivated by the latter's respiratory pipeline including lead drug Esbriet, which at that time was already approved in Europe and Canada. The acquisition preceded the FDA approval decision.

APPROVED THERAPIES FOR IPF

Name/Company	Mechanisms
Esbriet/pirfenidone/Roche/approved Europe: 2011, mild-to-moderate IPF, US October 2014, IPF	Blocks proteins including transforming growth factor (TGF)- ß, inhibits cellular and collagen proliferation and scarring and tumour necrosis factor (TNF)-α, which promotes inflammation. Approval based on 1,247 patients with IPF in three phase III, randomized, double-blind, placebo-controlled, multi centre trials. Meta-analysis of 1 year data revealed, pirfenidone reduced the proportion of patients with a ≥10% decline in % predicted FVC or death by 43.8% (95% CI 29.3–55.4%) and increased the proportion of patients with no decline by 59.3% (95% CI 29.0–96.8%).
OFEV/nintedanib/Boehringer Ingelheim/ IPF, Europe 2015, US 2014	Multi -kinase Inhibitor, blocks anti-fibrotic anti-inflammatory receptors, platelet-derived growth factor receptor (PDGFR) α and ß, fibroblast growth factor receptor (FGFR) 1–3, vascular endothelial growth factor receptor (VEGFR) 1–3, and colony-stimulating factor 1 receptor (CSF1R). Three pivotal studies in 1,200 people with IPF, one Phase II trial and two Phase III trials, compared OFEV 150 mg twice daily to placebo for 52 weeks. Resulted in consistent, statistically significant reduction in annual rate of decline in FVC with OFEV versus placebo of 68%, 52% and 45% respectively.

Source: Company data

Clearly these therapies are successful at reducing FVC and delaying treatment progression. However, there are limited data available on a conclusive benefit on overall survival. Both Esbriet and OFEV are used relatively interchangeably and care guidelines state that they are recommended for IPF sufferers with lung function of between 50% and 80% of their predicted value. However, treatment is stopped if disease progresses (a confirmed decline in percent predicted FVC of 10% or more) in any 12-month period.

In addition, both have treatment limiting adverse effects - in the case of Esbriet, nausea, rash and abdominal pain are common, the more serious side effects include elevated liver enzymes, photosensitivity and impaired gastrointestinal function. For OFEV the most common include severe diarrhoea, abdominal pain and nausea, which are sufficient in many cases to limit compliance.

Net sales of OFEV registered growth of 31.6% to €1,491m in FY19, and it has since been approved in two other fibrotic lung diseases, and rose 41.7 % to €975m in Q2, 2020, up from €677m in Q2, 2019, already surpassing consensus analyst estimates (c €800m by 2022). Esbriet registered CHF 1.1bn sales in FY20.

So, the unmet need remains immense despite the ability to slow disease progression, in particular for therapies with a better tolerability profile. There is still much to be learned, late diagnosis and hesitancy in initiation of treatment in earlier stage disease, understanding of how to manage and sustain therapy are all issues still to be uncovered. Reportedly up to 40% of patients go untreated, and this is partly down to a reluctance to prescribe medication given its side effects.

A COMPELLING RATIONALE FOR NXP002

NFX's lead programme NXP002 focuses on the area of IPF, although the underlying parent drug tranilast has broad prospects in a number of other indications owing to its anti-inflammatory and anti-proliferative properties seen in early-stage studies. These include the potential to inhibit fibrotic tissue and tumour formation, opening up the opportunity to meet unmet needs in a whole range of hard-to-treat diseases.

Originally tranilast was developed by Kissei Pharma (Market cap 109bn JPY) as an anti-allergy drug which inhibits the release of pro-inflammatory mediators and was approved in 1982 in Japan, China and South Korea. Subsequently tranilast was approved for dermatitis, allergic conjunctivitis, keloids and hypertrophic scars.

This compound belongs to the class of organic compounds known as n-cinnamoylanthranilic acids. These are aromatic compounds containing a cinnamic acid conjugated to an anthranilic acid.

Formulation challenges include the fact that tranilast is almost insoluble in water and unstable in solution and so despite its anti-inflammatory properties, Kissei was not able to make an aqueous solution for oral administration to leverage well documented preclinical efficacy seen in cancers and in fibrotic conditions. For treatment of chronic proliferative diseases such as fibrosis the drug delivery method to produce consistent, predictable drug levels at the site of action in the body that are maintained above the minimum effective concentration, is critical.

There are widely published, peer reviewed scientific papers showing its preclinical efficacy in vivo and in vitro in fibrosis and more specifically, in IPF. This is supported by a more recent study which tested tranilast in the bleomycin model. Bleomycin causes fibrosis in the lungs and the study demonstrated that tranilast significantly inhibits this lung fibrosis caused by bleomycin. Overall findings suggest that tranilast inhibits pulmonary fibrosis by suppressing TGFβ/SMAD2-mediated extra-cellular matrix (ECM) protein production, a major therapeutic target in IPF, presenting it as a promising and novel anti-fibrotic agent[4]. Furthermore, the SARS-CoV-2 pandemic is expected to greatly increase the demand for anti-fibrotic drugs due to the fact that **fibrosis can be a consequence of COVID-19 infection**[5].

There could be other attractive options to pursue, given the difficulty in treating fibrosis and those options include the as yet untreatable liver disease, non-alcoholic steatohepatitis (NASH) which affects up to 5% of the US adult population.

For now, the key focus is on the potential of NXP002 in IPF and here NFX is developing a new solid form of tranilast with a view to removing the barriers that have prevented reformulation in the past. Initially NFX is developing an inhaled form of tranilast to target pulmonary disease directly via the main site of fibrosis and inflammation. This is an innovative slant on repurposing tranilast as well as providing a differentiated mode of administration that can provide commercial advantages if the early promise is borne out, given the size of the market, lack of current treatment options and the opportunity to make an impact on disease progression.

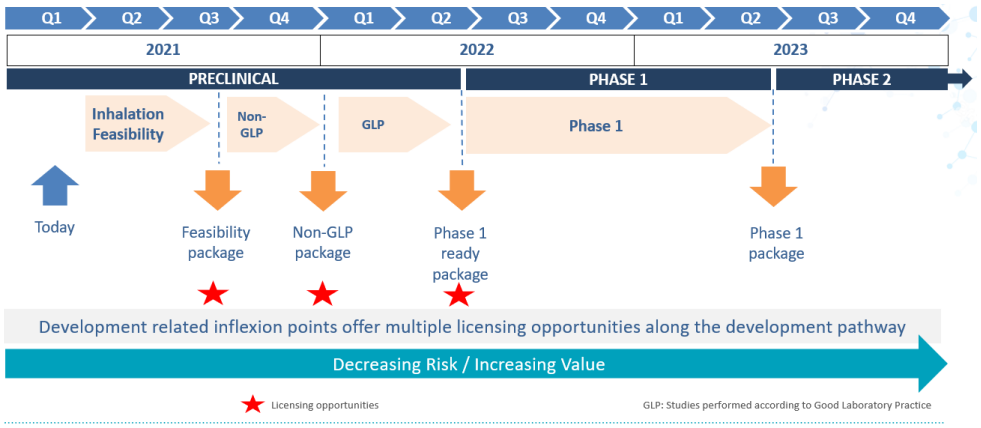
[4] Tranilast Inhibits Pulmonary Fibrosis by Suppressing TGFβ/SMAD2 Pathway in Drug Design, Development and Therapy 2020:14, Kato, M et al.
[5] Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy, Lancet Respir Med 2020, George et al.

MULTIPLE MECHANISMS AND A NEW DELIVERY ROUTE

NFX is developing NXP002 for IPF as the first indication, and ultimately this drug could be administered either in combination with standard of care to increase efficacy, or as a monotherapy for those unable to tolerate first line treatments, to help meet the acute need for alternative therapies to help slow disease progression.

NFX is preparing to put together a preclinical package for NXP002 in IPF, providing the opportunity on the successful completion of any or all of the three stages; Inhalation Feasibility, Non-GLP (Good Laboratory Practice) or Phase I ready, to seek global licensing opportunities. As we have said, the company has broad expertise in repurposing and drug development, especially for inhaled products, and is developing new drug forms with a versatile approach and flexible options.

TIMELINE AND KEY INFLECTION POINTS – NXP002 (INHALED TRANILAST)



Source: Nuformix

Adding value via inhaled delivery

NFX has particular expertise in inhaled therapeutics: CEO Dr Anne Brindley brings broad experience including a deep range of contacts drawn from the prior development and commercialisation of inhaled products, including Symbicort® and flutiform®, which are core products in a global asthma and COPD therapy market worth over $30bn[6] , including at inhaled products specialist Skyepharma (now Vectura) and at Glaxo, AstraZeneca and J&J. The particular benefits of inhaled therapies include:

- Delivery direct to the site of action for lung diseases, achieving drug levels in a high concentration in the target tissue to produce a therapeutic effect via a dose which is a fraction of the oral dose (inhalation doses are typically in micrograms vs oral doses of milligrams).
- Reduction in systemic side effects by virtue of the lower doses normally required to elicit a positive effect
- Avoiding liver metabolism to maximise the amount of drug available in the body to exert positive effects
- Faster onset of action directly to the main site of disease.

[6] Analyst estimate

- Successful precedent set in other lung diseases for example, asthma, COPD, Cystic Fibrosis, for a range of therapies (anti-inflammatories, bronchodilators, antibiotics)

- Potential for real therapeutic value-adding, not just extending the IP.

- The potential to complement standard of care administered via a different route e.g. oral medicines, as a combination treatment for lung disease like IPF.

NFX's initial focus is on developing a formulation of the drug to facilitate inhalation by the patient and intends to test the feasibility of rapid and deep penetration of the drug into the lungs using a nebuliser in the first instance during the early stage studies. While tranilast is generally well tolerated, uncommon adverse effects include liver and kidney problems that can be alleviated by reducing the dose. Nebulisation is an appropriate delivery system for a disease such as IPF, where lung function can be limited and additionally it is a cost-effect method of delivery especially for early studies.

Promising early data

There are limited, but promising, early data on NXP002 in preclinical lung tissue models, reported in December 2018, supporting the rationale in treating IPF and other fibrotic lung conditions. NFX carried out multi-patient tissue studies in partnership with Newcastle Fibrosis Research Group (NFRG) at Newcastle University, a renowned expert group in fibrosis disease models using a leading-edge human tissue model that closely replicates the clinical disease:

- Data demonstrates NXP002 inhibits fibrotic markers ex-vivo, even in very severely fibrotic patient tissue, giving strong support for treating IPF and other fibrotic lung conditions.

- In addition, NXP002 demonstrated specific action measured against key inflammatory targets that are relevant in IPF.

- NXP002 out-performed current standard of care treatment, pirfenidone (Esbriet).

Further, as recently reported, the combination of NXP002 with standard of care provided strong evidence of additional effects compared to standard of care alone on both fibrotic and inflammatory markers. In addition, the results showed evidence of similar or better activity of lower doses of standard of care in combination with NXP002, compared to higher doses of standard of care alone, indicating a potential for a dose-sparing effect of the combination.

COMMERCIAL POTENTIAL IN A HUGE AREA OF UNMET NEED

As we have said, the IPF pharmacotherapy market is worth $3bn across the largest populations of US, Europe, UK and Japan, currently shared by only two approved oral therapies. These therapies, although somewhat effective do come with a range of side effects and a proportion of patients do stop therapy due to tolerability issues Although there are a number of other promising targets in the pipeline, none are in the same class as NXP002 and most utilise a different mode of administration (oral or IV) compared to the inhaled NXP002. These factors and the severe nature of the disease leave room for additional innovative and disease modifying therapies.

The evidence that up to 40% of patients are not being prescribed disease delaying treatment indicates that there is still much more work to be done to help patients, plus much more to learn about the disease and its multiple drivers. In the words of one Key Opinion Leader, despite the benefits of current treatments, we *'still have a desperate need for drugs that make people feel better, that have fewer side effects, and that have a more profound impact on patient outcomes.'*

LATE STAGE COMPETITIVE LANDSCAPE FOCUS ON IPF

Drug/Company	Stage	Data
Pamrevlumab/Fibrogen (FGEN)/ Anti-CTGF antibody (IV route)	Phase III	Inhibits connective tissue growth. At Phase II, 103 patients randomly assigned (50 to pamrevlumab and 53 to placebo). Pamrevlumab reduced the decline in % of predicted *FVC by 60·3% at week 48
rhPTX-2; PRM-151/Roche (ROG)/ MREG differentiation stimulant (IV route)	Phase II	May 2019, data from 76 week open label trial, rate of decline in FVC % predicted reduced from -8.7% per year placebo to -0.9% per year on PRM-151. 6MWD** improved from -54.9 m per year on placebo to -3.5 m per year on PRM-151. Est 2023 filing.
PBI-4050/Liminal Bioscience (LMNL) (oral route)	Phase II	January 2017, open-label, single arm, exploratory, observational Phase II trial as monotherapy and + either nintedanib or pirfenidone, in 41 patients with IPF completed. Primary endpoints: safety and tolerability, secondary endpoints: change in pulmonary function, and inflammatory and fibrotic markers.
Inhaled therapies		
GB-0139/Galecto (GLTO)/small molecule inhibitor of galectin-3	Phase II/III	Dry powder formulation. Phase IIa studied plasma levels of prognostic disease biomarkers, YKL-40 linked to IPF mortality and CCL-18 linked to fall in lung function. These and several other biomarkers (PDGF-B, PAI-1, Galectin-3) fell in a dose dependent fashion from baseline in a consistent and statistically significant manner.
AP01 pirfenidone/Avalyn/Small molecule in aqueous solution	(Phase I/II)	Phase I study; safe and well-tolerated at a low dose in a group of 38 healthy volunteers and six IPF patients. An inhaled dose equivalent to 1/16 of the standard oral dose delivered 35 times higher peak lung levels of pirfenidone.
RVT-1601 cromolyn sodium/Respivant/Mast cell stabiliser	Phase II	Anti-inflammatory, delivered with a proprietary nebuliser. For cough associated with IPF
Nintedanib/Avalyn/ PDGF/VEGF/FGF inhibitor	Phase I	Aerosol formulation of nintedanib in salt solution, comprising water; nintedanib or salt thereof.

Source: Company data/**6 minute walking distance, *Forced Vital Capacity

There are around four other later stage inhaled/nebulised products in the pipeline, including reformulated Esbriet and OFEV being developed by Avalyn Pharma Inc. Judging by the rate of progress, one of the most advanced includes Fibrogen's Anti-CTGF mAb, pamrevlumab, delivered as an IV injection. The recent late stage failure of former front runner ziritaxestat/ Galapagos/Gilead narrows down the field somewhat. Analysts peg a market launch in 2022 of pamrevlumab and peak sales of up to $1.5bn.

The IPF patient population comprises approx. 350,000 people in the key countries and is growing at a rate of around 1.7% per annum and the US alone accounts for around 60% of cases. The size of treatment market is forecast to increase at a CAGR of 8% this decade along with incidence of new cases and with the projected approval of additional therapies to reach more than $4bn by 2030. There are a number of late stage candidates looking at a variety of biological pathways including those indicating inflammatory or fibrotic risk or which have prognostic value. A cross-section of the most promising are shown above. Note that many have Fast Track Designation and/or Orphan Drug Designation factors that can accelerate the review process and extend the period of market/data exclusivity and so this is also an option for NXP002.

GLOBAL MARKET OPPORTUNITY FOR NXP002

We look at the available market opportunity for NXP002 either as a monotherapy or as a combination therapy and in view of the changing landscape. As we have said NFX looks to take the programme to the next inflection point before seeking global business development opportunities. We consider that completion of the anticipated data packages, costing in aggregate approx. £2m over the next 18-months can be a major inflection point in terms of readiness for licensing and with an attractive market opportunity worth $3bn and growing, we calculate that NXP002 could command combined peak sales of £1bn in major markets.

OFEV and Esbriet have an average annual wholesale acquisition cost of $135k/$123k in US and around $65k in Europe. The patent expiry of OFEV and Esbriet could change pricing dynamics and so we use conservative assumptions, around 50% of prices of the incumbents, accepting that in reality this will be determined by clinical efficacy and side effect profile. On one side there will likely be more comparators in the market, but orphan disease status and differentiated modes of administration and mechanisms can justify pricing in line with the branded incumbents. A monotherapy is likely to attract higher pricing than a combination therapy, another factor that is yet to be elucidated.

Assuming that there is an approx. 0.05% prevalence in each population and assuming annual incidence of new cases of around 1.5% in Europe and US, with 60% diagnosed and 33% of the patient pool eligible for treatment, this equates to approx. 32,000 patients in US. 35,600 in Europe and 13,000 in Japan. At 33% penetration and an annual price of £52k in US, £24.5k in Europe and £38.5k in Japan, respectively gives a combined peak sales of £1bn for all major geographies, broken down as follows:

- US peak sales 32,000 x 33% x £52k = £544m
- Europe peak sales 35,600 x 33% x £24.5k = £288m
- Japan peak sales 13,000 x 33% x £38.5k = £164m

In the 'traditional' biotech model, drug development is a 10-year minimum process. With abbreviated timelines, a repurposed new physical form could be on the market as early as 2029 in US and Europe and 2030 in Japan following a bridging study, with patent expiry in 2038 (not including potentially available patent term extensions). We consider that the route of development and the fact that underlying drug is already known means that there is a higher likelihood of approval than via the standard drug development model, balancing the fact that NXP002 is a preclinical programme, but with the existing body of tranilast safety and PK data that NFX can leverage.

Considering that NFX is looking to prepare a package suitable for a global license deals for NXP002 in the main markets, this would position it to negotiate upfront, milestones and royalties with a partner proportionate with the stage of development. If it strikes a deal or deals at the preclinical stage then the return is likely to be a global deal package of around $360-450m, including upfront and milestones, plus mid to high single digit royalties on sales, based on recent market precedent, while there is potential for total deal value (upfront and milestones) to increase and royalties to rise to the mid-teens if a deal comes after NFX completes Phase I work on NXP002.

Beyond IPF, next steps in Fibrosis and Oncology

NFX has the option to investigate the scientific rationale for treating other diseases with NXP002 candidates for the broader fibrotic and oncology indications provided that the proof of concept is established This includes alleviating hyper-inflammation of the lungs in COVID-19 patients targeting the NLRP3 inflammasone, a key pathway in many inflammatory lung conditions such as Acute Respiratory Distress Syndrome (ARDS) and a

well-documented mechanism of tranilast[7]. The preclinical plan, which hinges on the feasibility and activity of NXP002 as delivered by the inhaled route, will also form a foundation for future studies in other lung diseases. There will be no additional expenditure allocated to other indications at the preclinical stage by NFX as firstly NFX is focussed on IPF as the disease target and secondly, several of the evaluation steps, including the confirming feasibility of administration via nebuliser and inhalation safety, would be the same for any lung disease.

Many of the epidemiological risk factors and biological processes that lead to viral-induced ARDS are shared with IPF. In addition, many of the current and emerging antifibrotic drugs could have therapeutic potential for treating severe COVID-19 and certain experts believe the burden of fibrotic lung disease following SARS-CoV-2 infection is likely to be high[8].

NFX has applied for a grant to advance the NXP002 programme via Innovate UK , and the outcome is due to be announced in Q1 2021. The company intends to seek further non-dilutive funding through further grant applications in the future.

There are other options to explore once a preclinical package on NXP002 is ready, in future, extending into new indications in which pulmonary inflammation or fibrosis are common factors offering significant commercial potential. NFX will be in a position to evaluate these options and business development opportunities once an effective data package is in place.

Other key areas to explore based on peer reviewed literature include:

- Oncology – Multiple in-vitro/in-vivo studies have shown the significant potential of tranilast in pancreatic, prostate and colorectal cancer.
- Fibrosis – NASH, kidney fibrosis, large markets with huge unmet need.

[7] https://pubmed.ncbi.nlm.nih.gov/29531021/
[8] Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy, Lancet Respir Med 2020, George et al.

NEW LIFE FOR A SUCCESSFUL CANCER SUPPORTIVE CARE DRUG

After NXP002, the next most advanced programme is NXP001 which shares the same API as Merck's globally marketed cancer supportive care treatment.

NXP001 is a Phase I co-crystal form of the NK-1 antagonist, aprepitant, which is the active ingredient in EMEND (Merck) marketed globally for the treatment of Chemotherapy-induced nausea and vomiting (CINV). NFX has developed Phase I data on the candidate showing that it is bioequivalent to EMEND.

CINV is one of the most crippling toxicities associated with cancer treatment, and up to 30% of all people suffering from cancer are advised to undergo chemotherapy and around 70% to 80% patients suffer from CINV. Managing CINV can mean the difference between a patient choosing and staying on chemo, successfully completing the course of treatment or discontinuing it.

NFX has a number of other options for the programme over and above CINV which are currently being evaluated under its agreement signed in September 2020 with the private company, Oxilio, which has an option to licence NXP001 for the development in oncology, rather than in oncology supportive care.

Aprepitant has a number of known properties, notably the NK-1 receptor is involved in cellular responses such as pain transmission and modulation of cell proliferation. Also it acts as a neuromodulator contributing to brain function associated with depression, stress, anxiety, and nausea. Its success in CINV is based on controlling the vomiting reflex. This compound has also shown antiproliferative properties in tumoral cell lines of glioma, neuroblastoma, retinoblastoma, pancreas, larynx, colon, and gastric carcinoma[9].

Existing data

In May 2019 NFX reported initial data from a pilot study of a proprietary co-crystal-based formulation developed within the NXP001 programme in healthy subjects, which demonstrated bioequivalence to Merck's EMEND at 125mg both in terms of peak exposure and overall exposure using the most well accepted measures, maximum concentration (Cmax) and Area Under the Curve (AUC). This was achieved without complex formulation, implying that there is room for adjustment in future.

There has been limited disclosure by NFX on the next steps and this is largely because Oxilio has the first option on NXP001 that will likely determine the next course of action and because NXP002 is the current priority. We assume that key points of differentiation might include overcoming problems with side effects include including tiredness, and GI impact. The co-crystal form may also overcome its insolubility and stability and offer a new mode of administration. For example, a liquid format rather than the capsule based EMEND could be valuable for severely ill, incapacitated people or to suit new treatment settings.

Oxilio oncology option

The terms of its option agreement signed in September 2020 with Oxilio cover a licence for the development and exploitation of NXP001 in oncology. Deal terms include an undisclosed up-front payment to NFX offering an exclusive option period of 6 months, within which a global licensing agreement can be agreed, expiring 24 March 2021.

Other than potential for global licensing for oncology indications, NFX provides no detail on the specific market being addressed under its alliance with Oxilio. We assume that ongoing evaluation includes assessment of the potential clinical and commercial rationale

[9] Biological and Pharmacological Aspects of the NK1-Receptor

for developing NXP001 in oncology as well as Oxilio's own strategic focus, resources and status.

If Oxilio exercises the option, NFX will negotiate a license agreement and licence its patent estate and know-how on NXP001 in return for an upfront payment and additional development milestones and a royalty on net sales, capped at £2m per annum. NFX also provided consultancy services to Oxilio during the option period. Oxilio will, if it exercises its option, develop NXP001 globally for the treatment of cancer and carry out clinical trials to determine which cancer types respond best to treatment.

If Oxilio decides not to exercise its option, NFX can reconsider its choices, likely via licensing options rather than pursuing further internal development of NXP001. We note that under the terms of the patent NFX has the opportunity to explore additional indications and to seek partners for indications including CINV, dermatology and addiction as well as oncology. We conclude that this is an opportunity to develop data, to carry out research with limited ongoing expense, and providing a source of near term income.

We will look again once the outcome of Oxilio's decision is known and once more is known about the cancer indication being pursued. If the option is not exercised, NFX will evaluate business development opportunities for NXP001 in oncology

NXP004 – REPOSITIONING A BLOCKBUSTER

NXP004 is an oral co-crystal form of an undisclosed oncology drug. The underlying drug is a blockbuster oncology therapy, a small molecule drug with mechanisms that could also have utility in fibrosis.

NFX is engaged in developing a robust and defensible IP position on NXP004, through generating more research data, before disclosing the underlying drug and seeking to license the IP.

NFX's strategy is to license the IP primarily for its existing oncology indications, as, in this case, the NFX IP on NXP004 could be of interest to the originator of the marketed drug as a means to extending its own patent estate to protect this high value drug in oncology.

Thus, NFX has the option to pass the technology and the new form back to the originator in order to extend the patent life of this high value drug in oncology. There is one patent application filed, and a second in progress – if granted, with potential expiry around 2041. Other licensing options include seeking a deal with a generic drug developer.

However in addition, we do know that there is already early but encouraging data from a preclinical pilot study on NXP004, reported in August 2020, in fibrosis.

The study evaluated NXP004 in human tissue in IPF compared to standard of care and focusing on the over-proliferation of extracellular matrix (ECM) components as a driver of IPF progression, differentiated from the main anti-fibrotic and anti-inflammatory mechanisms of NXP002/tranilast.

- NXP004 showed a dose-dependent reduction in the secretion of several key ECM components.
- These data suggest NXP004 compares favourably to current standard of care with regard to anti-fibrotic activity in this model.

The pilot study was interrupted as research partner Newcastle Fibrosis Research Group's (NFRG) facilities were commandeered on Government orders to support COVID testing.

While there is literature evidence for this drug's activity in fibrosis, the Company's strategy to derive most value for this asset is to pursue opportunities in oncology as a priority.

Other alliances

Ebers and Vistagen: Previously the Group announced two agreements with third parties centred on applying the Company's IP and performing fee-for-service work on their proprietary drugs. Whilst these agreements have provided Nuformix with undisclosed revenue and certain milestone payments, these agreements are not material for the Company's ongoing strategy or future revenue.

NXP002 Asia discussions: The Company is disappointed with the progress made to date with the business development activities in Asia. A new business development consultant has been engaged to assess the viability of legacy discussion coming to a successful conclusion in the near to medium term. It is the Company's strategy that in order to derive more value from the NXP002 asset, it is necessary to do further work to develop a more robust preclinical data package for NXP002 with the intention of building a data package that would be attractive for a global licensing deal.

Under previous R&D activities carried out on NXP001 in agreement with Newsummit Biopharma (NSB), NFX is still due payment of a £2.5m outstanding balance following a

dispute originating between NSB and its parent company, Zhejiang Yatai Pharmaceutical Co Ltd. The Company has pursued payment of this however the Company believes the probability of success of getting this payment is low.

The central internal focus of NFX is on developing value and accelerating licensing potential of NXP002 and advancing and evaluating the licensing options for NXP001 and NXP004.

FINANCIAL SUMMARY

We provide a summary of the historical performance of NFX.

Income Statement - Year End March - £'000	FY19	FY20
INCOME STATEMENT		
Revenues	610	535
Gross Profit	72	201
R&D Expenses	(1,449)	(525)
G&A Expenses	(438)	(595)
Operating Profit	(1,815)	(918)
EBITDA	(1,758)	(832)
BALANCE SHEET		
Current assets	347	796
Cash and cash equivalents	4	544
Other current assets	180	172
Non-current assets	4,288	4,331
Property, plant & equipment	28	83
Intangible assets	4,260	4,248
Current liabilities	(820)	(347)
Short-term debt	(15)	(38)
Accounts payable	(804)	(309)
Equity	3,815	4,743
CASH FLOW		
Operating cash flow	(299)	(718)
Investing cash flow	(27)	(43)
Financing cash flow	(7)	1,301
Proceeds from equity	-	1,338
Net increase in cash	(334)	540
Cash at start of year	338	4
Cash at end of year	4	544
Net cash at end of year	(11)	468

Source: Nuformix

- Revenues have been largely derived from consulting services, with well controlled expenditure via a lean virtual operating model.
- Negligible debt, intangible assets book value of £4.3m.
- NFX raised a total of £1.3m in FY 2020 via a placing. The gross cash balance at the end of September 2020, H1 2020 stood at £0.2m and NFX subsequently raised a further £0.6m in October 2020.
- The number of fully diluted shares in issue, including warrants and options, plus 78,250,000 to be issued shares, is 679,076,311.

FUNDING AND USE OF PROCEEDS

NFX has raised £1.565m gross (£1.4m net) by issuing 78,250,000 new shares at 2 pence per share, to progress its near-term strategy and the proposed use of proceeds is as follows:

- To support development of a preclinical data package for lead asset NXP002 for IPF.
- Staged investment approach with several options to license.
- Evaluate additional Business Development opportunities for NXP001 in oncology if the Oxilio option is not exercised.
- NXP004 – further research followed by Business Development.
- Additional working capital.

VALUATION

We evaluate the lead programme and look at recent deals in the IPF space to illustrate the value of NFX and its lead asset as it advances its strategy and/or secures new deals over the next 12-18 months. We use a DCF approach to value the lead programme NXP002 assuming global development and as it approaches key inflection points. We accept that this is the key focus and with the most certainty at present, until there is greater clarity on the way forward for NXP001 and for NXP004. We take into account that the programme is still at an early stage, nevertheless that risk is reduced owing to the existing body of safety data on the underlying drug, and because of the abbreviated regulatory route applicable for repurposed co-crystal or new solid form therapies.

For simplicity, we look at the value of the asset as if NFX were to market the product, rather than via a licensing deal, to illustrate its worth to potential licensees. Our valuation of NXP002 as a preclinical asset using a 13% WACC gives a risk adjusted valuation of NFX of £52.8m which is equivalent to 9 pence per share (based on 591.6m shares in issue post funding). This assumes that a Phase I ready package for the asset is in place which is being developed over the next 12-18 months, subject to funding. We illustrate the main assumptions regarding launch date, peak sales and pricing in each geography, using a 10% Likelihood of Approval for this programme alone.

NPV OF CASHFLOWS FROM NXP002 IN MAJOR MARKETS

Candidate	LOA*	Operating margin	Launch	Peak sales/annual price per patient
NXP002 US	10%	50%	2029	£544m/£52k/33% share of 0.032m population
NXP002 Europe	10%	50%	2029	£288m/£24.5k/33% share of 0.036m population
NXP002 Japan	10%	50%	2030	£164m/£38.5k/33% share of 0.013m population

Source: Analyst / *Low-average Likelihood of Approval, Phase I candidates: Source: BioMed Tracker

The de-risked global value of NXP002 in IPF is £528m, which illustrates its total value potential.

VALUATION OF NFX BASED ON RISKED ADJUSED NXP002

Programme	Value	Value per share
NXP002 Japan	£11.7m	
NXP002 Europe	£15m	
NXP002 US	£26m	
Shares in issue post financing £1.565m @ 2 pence/share: 591.6m	**£52.8m**	**9 pence**

Source: Analyst

NFX is looking to license the asset before Phase I, in which case we would anticipate a global deal value of between $360-450m, in upfront and milestone payments, plus single digit royalties on sales, increasing in value in proportion to the stage of development of the underlying asset: from feasibility up to the full Phase I ready GLP package, assuming successful outcomes and based on recent precedent. We illustrate a range of deal metrics in IPF to support our assumptions. Industry precedent shows that once a robust patent position is built, **even early stage IPF assets are attracting significant deals** in the indication. While pipelines are filling out, the novel approach, acute need and the inhaled route of administration are key factors that can differentiate NXP002.

IPF DEAL FLOW

Companies	Partner / date	Pipeline status at time of deal	Deal metrics (total value)
RedX (Licensing option) (RXC006: Porcupine (Wnt) inhibitor)	AstraZeneca/2020	Preclinical	$377m
Galecto (acquisition option)(TD139: Galectin-3 Inhibitor)	Bristol Myers Squibb/2014	Started first in human trial	$444m
Promedior (acquisition option)(PRM-151: rPentraxin-2)	Bristol Myers Squibb/2015Roche/2020	Phase II Phase II	$1,250 $1,390

Source: Company data

The deals illustrate the potential of NXP002 assuming it is partnered ahead of the clinical studies or indeed the value potential once more data are developed.

Clearly once further information is available regarding the way forward for the other programmes and alliances, we would look to revise our overall valuation assumptions.

Conclusion

NFX operates a relatively low risk and cost development model in which it is developing innovative forms of older drugs focused on high value commercial markets. In our view, a successful development of a preclinical package for the lead programme in IPF can be a differentiated and attractive target for licensing or acquisition by larger pharma players, judging by deal flow, market metrics and unmet need.

There is potential upside from licensing opportunities in NXP001 and NXP004.

NEWSFLOW

Over the next 12-18 months there are a number of possible events on the horizon:

- Initiation of the feasibility studies on NXP002 in Q2 2021
- Outcome decision on Oxilio option on NXP001.
- News on patent filing outcomes, strategic path and partnering for NXP004 in oncology.
- Outcome of Innovate UK Grant Application for NXP002 in Q1 2021.
- Potential completion (subject to funding) of Phase I ready package for NXP002 by H1 2022.
- Partnering news across the pipeline.
- Corporate: FY results 12 months ended 31 March 2021 – date estimated July/August.

BIOGRAPHIES

Dr Anne Brindley, Chief Executive Officer

- Over 30 years in Big Pharma and Biotech (GSK, AZ, J&J/Respivert, Skyepharma, Advent/AuroScience) with extensive expertise in respiratory and oncology R&D, and business development including in / out-licensing and M&A including company sale.
- Key role in successful inhaled products – Symbicort® (AZ) and flutiform® (Skyepharma).
- Extensive expertise in R&D in respiratory and oncology therapy areas - for innovator and generic products
- Former CEO Advent Pharmaceuticals Pty Ltd/ AuroScience Pty Ltd (Australia) with successful sale of the business

Dr Joanne Holland, Chief Scientific Officer

- Over 18 years' experience in R&D, IP & commercial roles within the pharmaceutical Industry.
- Expert in pharmaceutical solid forms, co-crystals, process R&D and drug reprofiling (Millennium, Stylacats). Leader in novel physical forms / cocrystal technology

Dr Karl Keegan, Non-Executive Director

- Over 25 years in life sciences. Over 25 years' experience in the life sciences sector
- CEO at HOX Therapeutics Ltd
- Previous roles included CFO, corporate development, M&A and finance
- 12 years as a highly regarded sell-side life sciences research analyst

Dr Julian Gilbert, Non-Executive Director

- Over 30 years of commercial and technical experience in the pharmaceutical industry
- Co-founder and former CEO of Acacia Pharma; Co-founder and Commercial Director of Arakis
- Led multiple business development projects

Ms Maddy Kennedy, Non-Executive Director

- Over 20 years of experience in the life sciences sector
- CFO at MyHealthChecked Plc
- Experience in IPO, M&A, fundraising and strategic review
- Previous roles included CFO at Alliance Pharma, Lab21, PsiOxus and Ieso Digital Health

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