Allenby CAPITAL

Company Note

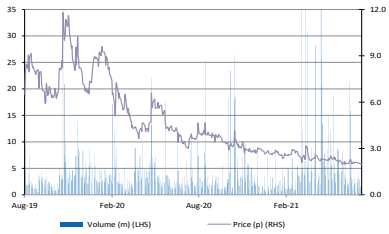
Full year results

15 July 2021

Corporate

Current price	**1.95p**
Sector	**Pharma & Biotech**
Code	**NFX.L**
Listing	**LSE – Standard List**

Share Performance



	1m	3m	12m
— NFX.L	-3.7%	-18.7%	-35.0%

Source: Thomson Reuters, Allenby Capital

Share Data		
Market Cap (£m)		**11.8m**
Shares in issue (m)		**591.6**
52 weeks (p)	High	Low
	4.65	**1.95**
Financial year end		**March 31**

Source: Company Data, Allenby Capital

Key Shareholders	
CPI Enterprises*	6.7%
Dr D J Gooding*	6.3%
Dr J M Holland*	6.3%
*Concert party (inc others)	28.0%

Source: Company Data, Allenby Capital

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Nuformix plc

Progressing NXP002 towards clinical trials

Nuformix is making good progress on the development of NXP002, its novel inhaled form of tranilast intended for idiopathic pulmonary fibrosis (IPF). It is executing a plan designed to generate a phase 1-ready formulation in c. 18 months' time, when it may be able to seek a licensing partner. IPF is an attractive market opportunity with around ten projects in mid/late-stage clinical trials, only two of which are delivered by inhalation, a route with self-evident advantages in this indication. The investment case, in our view, hinges on the potential economics of a future licensing deal for NXP002, although Nuformix does also have two other assets – one of which is in the process of being licensed. This report is, in part, intended to profile the landscape in IPF to guide investors as to NXP002's competitive position.

- **Preclinical studies show potential for single agent and combination use.** Data from an *in vitro* IPF model has shown anti-fibrotic/anti-inflammatory activity of NXP002 alone and in combination with two approved IPF drugs. These studies suggest the addition of NXP002 may achieve the same or better activity at lower doses of the approved drugs, which may offer advantages as both have challenging side effects. Additional preclinical studies are planned as Nuformix builds out a more robust data package.

- **Progress on NXP004**. Research is also underway on developing new forms of an undisclosed marketed oncology drug (with sales c.$1.5bn in 2020). A patent filed in 2020 may be granted in 2022.

- **Licensing deal under negotiation with Oxilio.** A licensing deal is being finalised with Oxilio, a private UK company, for NXP001, a novel formulation of aprepitant intended for cancer treatment.

- **Indicative value.** We believe a licensing deal or partnership for NXP002 as a Phase 1-ready asset for IPF could have a $360-450m headline value, although the upfront would be likely to be in the $10-20m range. Although, the economics of such deals are difficult to predict, the future NPV of this asset could be ~£50m. This future value would suggest the current fair value for Nuformix lies in the £10m to £20m range (1.7p to 3.4p/share).

- **Cash to 2023.** Nuformix results show net cash of £1.6m, giving a runway into late CY2022 based on our model.

Year End: March 31				
(£'000)	**2019**	**2020**	**2021**	**2022E**
REVENUE	610	535	196	50
ADJ. EBITDA	(2,734)	(833)	(1,220)	(1,365)
ADJ. PBT	(2,819)	(930)	(1,316)	(1,411)
ADJ. EPS (p)	(0.57)	(0.16)	(0.21)	(0.19)
CASH	4	544	1,670	688
EV/EBITDA (x)	N/A	N/A	N/A	N/A
PER (x)	N/A	N/A	N/A	N/A

Allenby Capital acts as Financial Adviser & Broker to Nuformix plc.

Investment thesis

Nuformix offers investors a play on the potential economics of a future licensing deal for NXP002, a novel inhaled version of tranilast repurposed for idiopathic pulmonary fibrosis (IPF) and other lung fibrotic conditions (including potentially COVID-related). Nuformix holds two patents the physical form of NXP002 and intends to generate additional IP and supporting data to build an attractive licensing package.

Identifying and developing repurposing opportunities in fibrosis and oncology

Nuformix specialises in identifying and developing repurposing opportunities in fibrosis and oncology. NXP002 is its lead programme and the main driver of value for investment purposes. In our view, NXP002 will present an attractive licensing opportunity, but we note Nuformix will have to find a partner at relatively early stage as it currently lacks the funds to undertake clinical trials. Given Nuformix's market capitalisation, it is possible a potential licensor may consider acquiring the company outright (to obtain full control of the IP), a scenario that could be attractive to Nuformix investors.

Sensitivities/risks

Nuformix is exposed to the risks typically associated with early-stage drug development, which may include the outcome of trials, although it is currently in formulation development. Although its target market of IPF is a characterised by high unmet medical need, it is also a highly competitive and, as such, Nuformix can be indirectly affected by the success (or failure) of competing programmes.

Nuformix intends to seek a licensing partner for NXP002 at the Phase 1 stage and, if successful, will still be entirely reliant on that company conducting all clinical development, registration and commercialisation of the resulting product. Although licensing deals are standard practice in the biotech industry, there is no guarantee that one can be struck for NXP002 and, if so, whether it can be done on attractive economic terms. The value that can be realised in a licensing deal is difficult to predict, as it is determined by multiple external (competitive) factors as well as the intrinsic qualities of the programme. The precedent deal values obtained in IPF may be greater for NCEs for than for a re-purposed asset at a similar stage.

Nuformix also operates fully virtually and has just one full-time employee, with all R&D and administrative functions performed under contract. It is therefore highly reliant on one individual. For investment purposes, its value is also entirely attributable to its lead programme.

Valuation

Fair value in the 1.7p to 3.4p/share range

We believe a licensing deal or partnership for a Phase 1-ready asset (in 18 months) for IPF could have a $360-450m headline value, although the upfront would be likely to be in the $10-20m range. The NPV of such a deal could be in the order of £50m. The economics of licensing deal are, however, very difficult to predict, as they depend on multiple factors. This future value suggests the current fair value probably lies in the £10m to £20m range (1.7p to 3.4p/share).

Financials

Cash at the year-end of £1.6m

Nuformix's financial results for FY2021 show revenues of £196k and operating expenditure of £1.4m, of which R&D was £0.4m. We expect this year to see some G&A cost savings this year, probably offset by higher R&D expenditure. Cash at the year-end was £1.6m, which should last to end CY2022. This investment case is not driven by financials except insofar as they constrain Nuformix's ability to fund R&D.

Formulation/repurposing specialist

Nuformix is a small, UK-based company that operates virtually and is focussed on the identification, development and exploitation of drug repurposing opportunities in fibrosis and oncology. It aims to identify and create IP around situations where known active pharmaceutical ingredients (APIs) can be reformulated in novel formulations, particularly using co-crystalline forms,[1] and then be developed for new indications.

Advance novel formulations to early value inflection points and license

Nuformix's business model is these advance novel formulations to early value inflection points and then license them to third parties for development, registration and ultimately commercialisation. Such early value inflection points may include preclinical studies in cellular or *in vivo* models. The reformulation aspect of the model is critically important as it provides intellectual property (IP) protection without which these opportunities would not be viable development propositions.

The investment proposition therefore hinges on Nuformix's ability to secure IP and license it to third parties and achieve an economic return. In the past, Nuformix has also provided some consulting services on co-crystal formulations on a fee-for-service basis, but this low-margin activity has now been discontinued.

Three R&D programmes

Nuformix currently has three R&D programmes, all of which are preclinical with one effectively Phase 1-ready. This latter project is subject to a licensing agreement currently being finalised with Oxilio, a small, privately-held UK biotech company. Nuformix's three current R&D programmes are summarised in Exhibit 1.

Exhibit 1: Nuformix R&D Portfolio

Programme	Lead Indication	Status	Notes
NXP002 (tranilast)	Idiopathic pulmonary fibrosis	Preclinical	Novel formulation of tranilast with improved characteristics suitable for inhaled delivery. IP consists of two patent families covering co-crystals and salts. Potential for use in other lung fibrosis conditions, including COVID-19-related lung fibrosis. Currently a liquid formulation is being optimised for use with a nebuliser.
NXP001 (aprepitant)	Oncology treatment	Phase I-ready	Co-crystal formulation of aprepitant with improved characteristics over the originator product (Emend, Merck & Co), expected to be developed for a cancer treatment indication. Emend is approved for approved for chemotherapy-induced nausea and vomiting (CINV) and post-operative nausea and vomiting (PONV). A PK study was conducted in 2019 with NXP001 in healthy volunteers, which reportedly showed bioequivalence to Emend in terms of peak blood concentration and overall exposure. A global licensing deal is currently being finalised with Oxilio, under which Nuformix will receive development milestones and a royalty on future net sales, capped at £2m per annum. PlusVitech, a Spanish biotech company, is also attempting to repurpose aprepitant in non-small cell lung cancer.
NXP004 (undisclosed)	Oncology	Preclinical	An improved formulation of an undisclosed cancer drug with 2020 sales ~$1.5bn, known to have a challenging side-effect profile. IP includes a patent application (made in 2020, but not yet granted)., which if granted, may provide commercial exclusivity to 2040/2041. A pilot study in 2020 examined the potential for repurposing in fibrosis, but subsequent commercial evaluation suggested the value was likely to be greater in oncology. Commercial options could include licensing to the originator (as a lifecycle extension) or to a generic company.

Source: Nuformix/Allenby Capital

Faster, cheaper and (relatively) lower risk

Finding new uses for known drugs

Repurposing is a drug development approach where known, approved and usually older, off-patent small molecule drugs are developed for new indications that were not known or not pursued for some reason by the originator. As an approach, it has certain advantages over *de novo* drug discovery that are especially applicable for small companies such as Nuformix. Essentially, it should be faster, cheaper and (relatively) lower risk in comparison with the development of a similar stage new chemical entity (NCE), albeit with greater commercial risk around the strength of IP and thus ability to price at a premium[2].

[1] This is an approach where two different chemical entities (the API and an inert excipient) can be crystallised together through non-covalent interactions. It can be used to enhance solubility and/or change other physical characteristics.

[2] See Alacrita, The-risk-reward-balance-in-drug-repurposing.

Since repurposed drug development programmes have an active molecule that is already well characterised, large scale studies used to confirm safety are not necessary. Pivotal studies are still required to establish efficacy in the new indication (specific medical use). Repurposing opportunities would also be likely to have a source of active pharmaceutical ingredient (API) commercially available, greatly simplifying what is often a costly step for small companies.

However, repurposing opportunities are only commercially viable where there is a way to obtain commercial exclusivity and prevent generic versions of original molecule from being substituted in the new approved use. In principle, a subsequently identified novel use for a known drug could be covered by a method-of-use patent, assuming it meets the normal hurdles for obtaining IP (non-obviousness, not anticipated by prior art etc). However, in practice this type of IP alone is not usually considered strong enough (i.e. patents can be circumvented or challenged) to justify development.

Need to ensure commercial protection

Hence, a viable repurposing programme will need further ways of ensuring commercial protection. This can be achieved by delivery of the active molecule in a new presentation (e.g. inhalation, when it the originator molecule is available orally) or when a technology is used that overcomes a particular formulation challenge (e.g. poor solubility). Both of these features are present in NXP002, the main focus of this report.

Commercial exclusivity can also exist because the original molecule was never launched in one or more of the key markets (and thus there would be no generic product available). Although it may at seem surprising, there are many pharmaceuticals that have only been developed or approved in certain countries or regions and were never launched globally. Tranilast is one such – it has only even been launched in Japan, China and South Korea – and was never approved in the US/EU. In these circumstances, its development may be more akin to that of an NCE, with correspondingly stronger commercial protection.

NXP002 – inhaled version of tranilast

NXP002 is a novel inhaled version form of tranilast intended for IPF[3] and potentially other fibrotic lung conditions. The new formulation (either a co-crystal or salt, Nuformix has been deliberately vague about this) improves the otherwise poor solubility of the existing oral product. In our view, Nuformix's IP should be sufficiently strong to make for an attractive development opportunity, as it has three aspects that potentially provide commercial exclusivity: the formulation IP, the novel route of administration (inhalation) and the fact that tranilast is not available in two of the three main regions (i.e. US/EU).

Tranilast

Tranilast does, however, have a long history of safe use. It was originally developed by Kissei Pharmaceuticals of Japan and launched (as Rizaben) in oral dosage form for asthma in 1982. Its indications were later extended to keloids and hypertrophic scarring, both fibrotic conditions affecting the skin, in 1993. An eye drop formulation was approved in 1995 and is widely used for allergic conjunctivitis. It is now generic in Japan.

In addition, Kissei, in collaboration with the then SmithKline Beecham, conducted a large, but unsuccessful, global Phase 3 study of tranilast in 1999-2001 for the prevention of restenosis associated with coronary intervention, the results of which were published in 2002[4]. All further development by Kissei appears to have been discontinued at this time.

Other repurposing efforts involving tranilast

Tranilast has been the subject of prior attempts at repurposing, most recently by a private but now apparently moribund, US biotech Nuon Therapeutics. Nuon entered into a

[3] Idiopathic is used to describe a condition which arises spontaneously or for which the cause is unknown.

[4] see Holmes *et al*. Circulation. 2002;106:1243–1250.

licensing deal with Kissei in 2007 (presumably in part to access Kissei's non-clinical and clinical data for regulatory purposes) and conducted two Phase II studies with its oral form (NU1618) for hyperuricaemia associated with gout in 2010-11. The smaller of these studies was reported to have rendered a positive result[5], but no details were ever reported of the outcome of the larger study (and thus the outcome can be speculated to have been negative). Nuon also listed an EU trial for rheumatoid arthritis in 2008.

Fibrotech, an Australian biotech spun out from the University of Melbourne, conducted early clinical studies with FT011, an orally available analogue of tranilast, in diabetic nephropathy. Promising early results lead to the company being acquired by Shire Pharmaceuticals in 2014 (for US$75m with US$482.5m of contingent payments), although the project was later discontinued. Certa Therapeutics, an Australian biotech with the same founder as Fibrotech, bought back FT011 from Shire in 2018 and is now conducting a Phase 2 study in systemic sclerosis. This study is testing 200mg and 400mg doses of FT011 (compared with a 600mg approved dose of tranilast). An analogue is not strictly a repurposing programme, as FT011 has a composition-of-matter patent, but this programme could, in theory, be explored in lung fibrosis in the future.

There are four studies listed on clinicaltrials.gov as currently underway involving tranilast, as an oral formulation, all for rare inflammatory skin conditions (mucinoses, scleroderma, sarcoidosis and cryopyrin-associated periodic syndrome). These are being conducted by a several Chinese hospitals; the uses also appear to be covered by patents in China, issued to these bodies.

Allenby Capital has not found any other R&D involving tranilast underway by commercial organisations.

Orphan drug status

Orphan drug designation (ODD) could become a fourth pillar by which Nuformix could gain commercial protection for NXP002, as well as providing other useful benefits. ODD is a legal status that can be applied to a product if it is intended to treat a sufficiently small population, which would be the case in IPF. The legislation was brought it in to incentivise development for conditions where limited patient numbers would otherwise make development uneconomic. In the US, ODD provides the sponsor with tax credits for clinical trial costs and a waiver of user fees at the FDA. It also provides commercial protection by precluding regulators from approving any products with the same API/indication for a fixed period of time after approval.

Well-established business model

Developing orphan drugs is a well-established business model within biotech because the small patient populations mean that drugs can be developed faster (trials are smaller, only one efficacy study is usually required), regulators look more favourably on surrogate markers and, most importantly, pricing in the market is much higher. The two approved IPF products, which both have orphan drug status, are priced at ~$100k per patient per year, and this would be a reasonable guide for NXP002. Indeed, because of these factors the return on investment for pharmaceutical R&D in orphan conditions is probably considerably higher than that in non-orphan ones.

There are no ODDs covering tranilast in IPF, but two are in existence covering in other indications, although, as noted above, neither is supporting active development. The first US orphan drug designation was issued in 2003 to Angiogen Pharmaceuticals, an Australian company, for malignant glioma; Angiogen appears to have been at some point acquired by Nuon Therapeutics. The other was issued in 2010 for prevention of scarring in post glaucoma filtration surgery to Altacor, and later transferred to Voisin Consulting, a life sciences consulting firm.

[5] See press release link.

Nuformix is likely to seek ODD status for tranilast for IPF in due course.

Patents

Two patent families

Nuformix has two patent families covering various tranilast co-crystals[6] and salts, but it has not disclosed which is being used NXP002. It does not have (and probably would probably not be able to obtain) a method-of-use patent.[7]

The company has generated some supporting data from preclinical studies performed by the Newcastle Fibrosis Research Group at Newcastle University, UK. These studies examined anti-fibrotic and anti-inflammatory activity (ie by measurement of fibrotic and inflammatory markers) of NXP002 alone[8], and in combination with two approved IPF drugs, in precision-cut human lung slices from an IPF patient post-lung transplant. Results reportedly show single agent activity and evidence of additive effects for combinations of NXP002 with Esbriet (pirfenidone, Roche) and separately with Ofev (nintedanib, Boehringer Ingelheim). In addition, Nuformix claimed the data suggest it may be possible to achieve similar (or better) activity at lower doses of the approved drugs when used in combination with NXP002 than the higher doses of the two drugs when used alone, indicating a potential for a dose-sparing effect.

Nuformix has confirmed to Allenby Capital that the study used NXP002 (and not simply tranilast) but it is not known how the dosages used were determined to be representative of physiological levels with inhaled NFX002 and orally delivered Esbriet and Ofev in IPF patients.

Current development activities

NXP002

Nuformix has sourced supplies of NXP002 for use in formulation development activities, for nebulisation feasibility studies and in vivo studies. It is conducting preclinical pharmacokinetic and pharmacodynamic studies in relevant in vivo models that are designed to demonstrate that NXP002 has appropriate properties for use as an inhaled therapy for IPF. These studies, once complete, will collectively form an inhalation feasibility package. This work will then shift towards development of a liquid formulation suitable for use with a nebuliser with desirable pH, osmolarity etc so that it can be used safely in patients, and other characteristics so that an aerosol has the right droplet size for accurate and consistent delivery to the lung. Once completed, Nuformix could use an off-the-shelf nebuliser to test a product and/or engage with a developer of a more specialised nebuliser (e.g. Monaghan Medical, Vectura, Phillips, Omron or Pari International).

Nuformix has not published any of its work to date, in part for reasons of commercial sensitivity. However, a paper published last year by Japanese academic researchers (Kato *et al*) provides some independent scientific support to the project. The authors reported the results of a study investigating *in vitro* effects of tranilast on extracellular matrix production and the TGFβ/SMAD2 pathway in human alveolar epithelial cells, with *in vitro* observations validated in a murine pulmonary fibrosis model. The authors concluded that tranilast is a promising and novel anti-fibrotic agent for IPF.

Timelines for NXP002

Nuformix expects to complete the development of the liquid formulation by the end of this year, by which point it will be able to conduct non-GLP toxicology studies of the inhaled product, which will be required for the change of route of administration. This will be in two different species. On completion of these studies, towards the end of 2022, it

[6] These are unlikely to be exhaustive of all possible co-crystals with tranilast.

[7] There are a number of academic publications discussing anti-fibrotic activity of tranilast dating back to the 2000s, which would be considered prior art.

[8] No data have been published yet (the assertions are based solely on descriptions of the outcome in a press release).

should be in a good position to seek a licensing deal, although it is possible this could be achieved earlier.

We note that at that time it may be attractive/possible to raise the (relatively modest) funding needed to conduct some early studies in healthy volunteers (including elderly/smokers) and IPF patients to establish PK/PD parameters and reach the next value inflection point. These studies would probably take two years to conduct and would be aimed at establishing a dose and a strategy for use in combination with existing agents (such studies in patients would typically have a treatment period of 12-24 weeks and thus take at least a year to undertake).

This point (c2024) would have to have a licensor involved as it would require an important decision over whether to develop NFX002 for use in combination with the then standard of care (SoC), perhaps to allowing dose reductions of difficult to tolerate therapies, or as a monotherapy in patients who have discontinued SoC therapy. This will obviously depend on a commercial analysis of the market, which would be conducted then and informed by the therapeutic landscape at that point.

We anticipate it would require up to a year to plan and initiate a pivotal study (to allow for engagement of a CRO, identification of investigators, and ethical review etc). This study would be likely to require two years (at a minimum) to conduct from first patient in, since it would probably have an endpoint at 48 weeks of dosing (this is the regulatory standard). On this basis, the earliest that a registration dossier could be filed would be 2028, with approval and launch in 2029. We note that studies could be smaller than those typical of NCE competitors, as there would be less requirement to achieve a level of certain patient exposure for safety. It is also possible that a well-funded big pharma partner could improve on this, by conducting some development activities in parallel.

Inhalation as a route of administration

Given the nature of IPF, inhalation seems to be the most obvious way to deliver the active agent, as it should allow high local concentrations of an active agent in the lungs where the fibrosis occurs, with minimal systemic exposure. However, it is more difficult to develop products for inhalation and it does not appear to have been done for either of the two approved agents when initially under development by their originators. Given Boehringer Ingelheim's R&D expertise in the respiratory area, we can presume it may have tried this unsuccessfully. It is possible this was not found to be feasible with the API formulations because of poor solubility or for other reasons.

There remains an obvious opportunity to develop new formulations of pirfenidone and nintedanib for inhalation and the privately-held US biotech firm, Avalyn Pharma, has done precisely this (although it is understood not to be using novel drug formulations). Avalyn recently reported mid-stage clinical trial data showing a dose response for its lead product, AP01 (pirfenidone, using the eFlow nebulizer from PARI Pharma).[9]

Avalyn study

The Avalyn study suggested a dose of 100mg twice daily delivered by inhalation can improve lung function compared with Esbriet, which has an approved dose of 267mg, taken three times a day (or 801mg in total per day). A Phase 1 study had earlier suggested that a single 100mg dose delivers a 35-fold higher local concentration (Cmax) in the lung epithelium than was achieved with 801mg orally. The same dose also had 15-fold lower systemic exposure, which is likely to be correlated with side effects and tolerability. These

[9] Data disclosed in the press release the study tested two doses, 50mg once daily and 100mg twice daily for 24 weeks. The high dose group showed no loss of lung function, as measured by FVC, while the low dose group had a progressive loss, a difference that was statistically significant (p=0.049).

data illustrate the degree of improvement that could be obtained with an inhaled version relative to an orally delivered one.

Avalyn has also published preclinical data on its inhaled nintedanib formualation, AP02. We presume it has prioritised AP01 over AP02, because of the earlier patent expiry on pirfenidone. Avalyn has raised a total of $97.5m in two VC funding rounds, most recently in 2020, which would suggest it has a post money valuation of $150-200m.

IPF

IPF is a devastating disease associated characterized by restriction in lung capacity caused by scarring of lung tissue for unknown reasons. It has a median survival of just 3 years and the only curative treatment option is lung transplant, but lack of donor organs (and cost) means this is not an option for most patients. There is significant unmet medical need in IPF for better tolerated agents and, ones that can stop or reverse the loss of lung function.

Approved products for IPF

The two products are currently approved for IPF, Esbriet and Ofev, which are well established but have only been shown to slow the rate of decline in loss of lung function and have not demonstrated a survival benefit. Both drugs also have challenging side-effects, which is thought to contribute to the fact less than 50% of IPF patients are on treatment. Esbriet was launched first in 2011, followed by Ofev in 2014. Both drugs are used relatively inter-changeably and guidelines recommend them for IPF patients with lung function of between 50% and 80% of predicted value. However, treatment is stopped if disease progresses (a confirmed decline in predicted FVC of 10% or more) in any 12-month period.

Ofev is more widely used agent and its sales are also growing much faster (38% vs 4% y-o-y for Esbriet in 2020). The two drugs have combined sales of $3.7bn, which approximates to the market for IPF. The market is forecast to grow by 7.3% CAGR to $8.8bn by 2027. The two products are profiled in the table below.

Exhibit 2: Approved therapies for IPF

Name/Company	Approval	Notes
Esbriet (pirfenidone) Roche	Approved in EU in 2011 and US in October 2014	Blocks proteins including TGF-ß, inhibits cellular and collagen proliferation and scarring and TNFα. Has orphan drug status in EU (providing ten years market exclusivity expiring 28/2/2021). Sales were $1.2bn in 2020. The composition of matter patent expires in 2021 although subsequent patents may provide further protection. Generic challenges are however underway. Suffers poor tolerability, particularly nausea and dizziness and ~50% of patients discontinue, dose adjust or switch to Ofev.
Ofev (nintedanib) Boehringer Ingelheim	Approved in US in 2014; EU in 2015.	Multi-kinase Inhibitor that blocks anti-fibrotic anti-inflammatory receptors, PDGFR α/ß, FGFR1–3, VEGFR 1–3, and CSF1R. Also approved for systemic sclerosis associated interstitial lung disease (SSc-ILD) and chronic fibrosing ILDs with a progressive phenotype. Nintedanib is also approved (as Vargatef) for non-small cell lung cancer. Ofev sales were $2.5bn in 2020, primarily in IPF. Boehringer Ingelheim is conducting a Phase3 trial of Ofev in Covid-19-induced pulmonary fibrosis. Earliest date for generic entry is June 7, 2029. Most common include severe diarrhoea, abdominal pain and nausea.

Source: Allenby Capital

IPF pipeline

We consider it important to monitor the therapeutic landscape in IPF as part of investment analysis, as the strength of the competition will be a major factor that will determine the terms of any future NXP002 licensing deal. It also allows an assessment of how and in what combination the product will have to be tested (since pivotal trials will have to test the drug in combination with the then standard of care) as well as the likely size of those studies.

Our analysis of the industry pipeline suggests there are nine programmes in active mid- and late-stage clinical trials, including three in Phase 3. We have only included those projects with active trials underway that are both randomised and use the regulatory

endpoint, Forced Vital Capacity (FVC), to measure treatment effect[10].This pipeline is shown in Exhibit 3.

Exhibit 3: IPF Pipeline

Company	Drug	Mechanism/description	Stage	No of pts	NCT ID	Data
Fibrogen	pamrevlumab	IV administered (Q3w) mAb against CTGF.	Phase 3	340 +340	NCT04419558/ NCT03955146	Jan-23/ Apr-23
Roche	RG6354 (PRM-151)	IV administered (Q4w) human pentraxin-2	Phase 3	658	NCT04552899	Feb-23
United Therapeutics	Tyvaso (treprostinil)	Inhaled prostacyclin analogue (3x/day)	Phase 3	396	NCT04708782	Jun-24
Suzhou Zelgen Biopharmaceuticals	Jaktinib	Oral JAK inhibitor	Phase 2	90	NCT04312594	Oct-21
Boehringer Ingelheim	BI 1015550	Oral. Mechanism not disclosed.	Phase 2	150	NCT04419506	Oct-21
Pliant Therapeutics	PLN-74809	Oral αVβ6/αVβ1 integrin inhibitor	Phase 2	84	NCT04396756	Dec-21
Bristol Myers Squibb	CC-90001	Oral JNK inhibitor	Phase 2	210	NCT03142191	Sep-22
Galecto Biotech	GB0139	Inhaled galectin 3 inhibitor	Phase 2*	500	NCT03832946	Dec-22
Bristol Myers Squibb	BMS-986278	Oral LPA1 antagonist	Phase 2	360	NCT04308681	May-23

Source: Allenby Capital;* Galecto believes this trial may be sufficient to support an accelerated approval.

The industry IPF pipeline lost what had been its lead programme in April this year when Galapagos (Euronext/Nasdaq: GLPG) and its partner Gilead Sciences (Nasdaq: GILD) discontinued ziritaxestat, following an adverse interim safety review. The two Phase 3 trials had been due to report results at the end of this year.

This meant the lead position effectively passed to Fibrogen (Nasdaq: FGEN) with pamrevlumab, which is conducting two Phase 3 trials that started in 2020 and are due to read out in 2023. Results of these are keenly awaited, as Phase 2 trials have been the first to show evidence of functional improvement,[11] that an open-label extension suggested could reach out to 76 weeks.

Roche initiated a Phase 3 study codenamed STARSCAPE for PRM-151 earlier this year, with data expected in 2023 (highlighting the fact that big pharma can expend more resources on a project to recruit patients faster). It has shown a slowing of loss of lung function and stabilisation on the six-minute walk test at 24 weeks.[12]

Fibrogen's studies enrol only patents who have discontinued Esbriet or Ofev, while the Roche's recruits those stable on standard of care (SoC) as well as those who have discontinued the approved drugs, which means it can access a wider pool of patients. Both drugs are also being examined in other indications: Fibrogen has Phase 3 trials with pamrevlumab for cancer and Duchenne muscular dystrophy; the Roche drug is in Phase 2 trials for myelofibrosis.

United Therapeutics (Nasdaq: UNHR), has just started a Phase 3 programme with Tyvaso, which is notable both because it is inhaled and is already approved in other indications – it is sold for pulmonary hypertension associated with interstitial lung disease (PH-ILD) and pulmonary arterial hypertension. United Therapeutics is studying a high dose of Tyvaso in

[10] FVC is a measure of the ability to inhale and exhale and 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.

[11] Pamrevlumab, an anti-connective tissue growth factor therapy, for idiopathic pulmonary fibrosis (PRAISE): a phase 2, randomised, double-blind, placebo-controlled trial. Lancet Respir Med 2020.

[12] Effect of Recombinant Human Pentraxin 2 vs Placebo on Change in Forced Vital Capacity in Patients With Idiopathic Pulmonary Fibrosis: A Randomized Clinical Trial, JAMA 2018.

IPF, the same as used in PH-ILD (9-12 breaths, 4 times per day), while PAH uses a lower dose (3 breaths, 4x daily).

In the study (and in use in PH-ILD), patients are started at 3 breaths per administration and encouraged to titrate up to 9-12 breaths over 8 weeks, depending on their ability to tolerate side-effects. The Tyvaso IPF study recruits those patients on SoC as well as those who have discontinued. The current Phase 3 study was initiated after a post-hoc analysis of data from a Phase 2 study showed a positive impact on FVC in IPF patients with pulmonary hypertension.

Aside from Tyvaso, Galecto's GB139 is the only other inhaled product currently in the later-stage IPF pipeline and is also something of a wild card. The Swedish company believes its Phase 2 trial may be able to support an accelerated approval in patients who cannot tolerate Esbriet or Ofev, despite a setback earlier this year. This occurred when the company had to discontinue the higher dose and combination with SoC arms, after an interim review at 278 patients pointed to an adverse safety profile. The study will now recruit only into the lower dose 3mg/day arm, probably with 2:1 randomisation. We estimate this change will mean the study will render data from c178 patients on the lower dose, in comparison with 133 on placebo.

We expect the mid-stage pipeline to expand later this year, when Galapagos starts a planned Phase 2 trial with its oral CHIT1/AMCase inhibitor, GLPG4716 (formerly OATD-01, in-licensed from OncoArendi (WSE: OAT)). Given Galapagos' strong funding position and ambitions in IPF it can be expected to move this asset forward aggressively. Earlier this year, Galapagos discontinued a separate internally-generated candidate, GLPG1205, despite positive Phase IIa trials, in favour of advancing GLPG4716.

We would also expect Avalyn to move quickly to a pivotal study of AP01, adding a third inhaled programme to the industry pipeline. It faces an interesting strategic dilemma of whether to pursue a fast-to-market approach that would define AP01 as closely broadly an inhaled version of Esbriet or pursue a more ambitious one that would take longer but position the drug entirely on its own merits. The latter would require, among other things, a complicated Phase 3 design, perhaps with a double-dummy with cross-over.

There are several companies pursuing repurposing efforts in IPF at the early clinical stage, notably Vicore Pharma of Sweden and Algernon Pharmaceuticals in Canada. Vicore is developing a version of thalidomide, while Algernon is developing ifenprodil, a drug approved in Japan for peripheral circulatory disorders.

Although not a repurposing programme, Puretech Health (LSE/Nasdaq: PRTC) is aiming to advance LYT-100 (deupirfenidone) to Phase 2 studies for IPF this year. This product is a deuterated version of pirfenidone with potentially better PK properties than the original molecule, possibly with improved tolerability. Puretech claims Phase 1 studies showed a 25% improvement in Cmax and 35% increase in AUC versus pirfenidone.

Other companies are developing products that have been in development for other indications but are not approved anywhere. Kinarus Pharmaceutiacals, a privately held Swiss biotech, is one such. It is developing a combination of pamapimod, a p38 MAPK inhibitor, with a PPAR agonist (probably pioglitazone). Pamapimod was licensed from Roche, which tested it in rheumatoid arthritis but discontinued development in c2005. Kinarus states KIN001 is ready to enter Phase 2 for IPF.

NeRRe Therapeutics is developing orvrepitant for chronic cough associated with IPF. This project is particularly relevant for Nuformix, as orvrepitant, although never approved (it was under development by GlaxoSmithKline for depression) has the same mechanism as aprepitant, the originator molecule for NXP001. The German biotech Pieris (Nasdaq: PIRS)

is developing an inhaled Anticalin product, PRS-220, for IPF and potentially Covid-related lung fibrosis with clinical trials expected to start next year.

Valuation

Fair value range of 1.7p to 3.4p/share

Allenby Capital considers the large majority of Nuformix's value to lie in NFX002. Assuming it is able to seek a licensing deal for NFX002 as a Phase 1-ready asset (in perhaps 18 months), we believe it could perhaps achieve a deal with a $360-450m headline value, although the upfront would be likely to be in the $10-20m range. The NPV of such a deal could be in the order of £50m, assuming a 10% probability of success and a 13% WACC. This future value suggests the current fair value probably lies in the £10m to £20m range (1.7p to 3.4p/share).

The table below summarises deals in the IPF space in recent years and may give an indication of terms that may be possible for a licensing deal.

Exhibit 4: Licensing deals and M&A in IPF

Licensor/programme	Partner / date	Development status	Deal terms.
RedX Pharmaceuticals RXC006	AstraZeneca/ 2020	Preclinical	Up to $17m in "early payments" (signing, and on milestones up to the start of a first clinical trial), of which first $4m received in June 2021. Up to $360m in additional development and commercial milestones plus tiered royalties (mid-single-digit).
OncoArendi/ GLPG4716 (OATD-01)	Galapagos/ 2020	Phase 2ready	Upfront payment of €25m with development, regulatory and commercial milestones of €295m, for a total deal value of €320m, with tiered royalties ranging up to low double-digits.
Teva/SD-560 now LYT-100 (deuterated pirfenidone)	PureTech Health/ 2019	Preclinical	Acquired for a non-material upfront, $84m of developmental, regulatory and commercial milestones and low- to mid-single-digit royalties on sales (for 10 years). Teva obtained this programme as part of acquisition of Auspex Pharmaceuticals in 2014.
Bridge Biotherapeutics/ BBT-877	Boehringer Ingelheim/2019	Phase 1	Global license deal with a near-term payment of €45m and up to E€1.1bn in milestones. The deal was terminated in 2020.
Afferent/ (AF-219, now MK-7264)	Merck & Co/ 2016	Phase 2	Purchase consideration of $500m, with a further $750m based on the outcome of Phase II trials. Development switched to chronic cough associated with IPF; now filed in this indication following positive Phase 3 studies.
Galecto/ (TD139/GB139)	Bristol Myers Squibb/2014	Phase1	Option to acquire company for a headline $444m, including option fee, option exercise fee (upfront) and other milestones, which was never exercised.
Morphic/ MORF-720 and MORF-627	Abbvie/ 2014	Preclinical	AbbVie paid $100m for an option to multiple fibrosis targets in 2014 and $20m to exercise an option twice.
Promedior (PRM-151: rPentraxin-2)	Roche/ 2019	Phase 3 ready	Acquired for an upfront payment of $390m, with development, regulatory and commercial milestones of up to $1bn. In 2014, Bristol Myers Squibb paid $150m for an option to acquire Promedior, which was never exercised.

Source: Company data

Sensitivities/Risks

We identify a number of specific risks and uncertainties that investors should consider in relation to the Nuformix.

Uncertain outcome of clinical trials. Significant scientific and clinical risks should be assumed to exist early-stage drug development, including major risks over the outcome of clinical studies.

Highly competitive markets. Development of new drugs for IPF is highly competitive and standards of care can and will likely change based on the success of competing molecules. NFX002 is most likely be used in combination with one of these existing standards of care.

Lack of composition of matter IP. Commercial exclusivity will rely on several factors, but not a fundamental or composition of matter patent. It is therefore theoretically possible, although unlikely, for another company to develop the same repurposing opportunity for an inhaled formulation of tranilast for IPF or another indication that may undermine the commercial attractiveness/business case.

Limited resources (financial and human). Nuformix has relatively limited financial resources and more importantly just one employee, using a network of consultants for R&D and administrative activities. We note it has no business development manager (normally important for licensing deals) or R&D project manager, with both activities currently performed by the CEO.

Requirement to find a licensing partner. Nuformix will have to find a partner for NXP002, but there is no assurance it will be able to do so and, if so, what economic returns it may provide. The value that can be realised in a licensing deal is very difficult to predict, as it is determined by multiple external (competitive) factors as well as the intrinsic qualities of the programme.

Reliance of a partner. Assuming a licensing partner can be found, Nuformix will be highly reliant on this company to complete clinical development, obtain registrations and commercialise any resulting products.

Financials

Nuformix's financial results for FY2021 show revenues of £196k and operating expenditure of £1.4m, of which R&D was £0.4m. We expect this year to see some G&A cost savings, probably offset by higher R&D expenditure. Cash at the year-end was £1.6m, which should last to end CY2022. This investment case is not driven by financials except insofar as they constrain Nuformix's ability to fund R&D.

We are publishing a model with forecasts for FY2022, showing notional revenue of £50k (vs £196 in FY21), G&A costs (before share based payments) of £780k and R&D of £500k. R&D is mostly a discretionary item and the level of expenditure could be increased if funding permits, for example from receipts from licensing deals.

The March 2021 fundraising circular noted an unpaid £2.5m in license fees due from Newsummit Biopharma relating to NXP001. The accounts do not make provision for the this. The license has been terminated for material breach[13], and is unlikely ever to recover the sum (it also cannot justify the cost/risks of trying to seek legal redress).

In the past, Nuformix has operated a fee-for-service consultancy business in co-crystal formulations, but this has now been discontinued (there were not revenues in the second half of FY2021). In 2019, IP related to novel forms of a cannabinoid was licensed to the Canadian company Ebers Tech, in a deal that provided up a modest upfront and up to £51m R&D and milestone payments, plus 20% royalties on sales. Ebers is currently being acquired by Kelly Ventures (TSX-V: KKL.P), a "pool company" (i.e. shell company or SPAC).[14] The project has completed and realistically no further sums are considered likely to be received.

[13] Newsummit Biopharma is listed on a financial website as being out of business. Its website is no longer functional.

[14] This was last reported on 30 June on the Canadian securities filing database SEDAR. Note Kelly Ventures has a market capitalisation of C$712k.

Exhibit 5: Summary financials				
Year-end: March (£000s)				
Income statement	**2019**	**2020**	**2021**	**2022e**
Revenues	610	535	196	50
Cost of goods sold	-538	-334	-62	0
Gross Profit	72	201	133	50
R&D Expenses	-1,449	-525	-363	-500
G&A Expenses	-438	-488	-953	-803
Underlying Operating Profit	**-1,815**	**-812**	-1,183	-1,253
Share based payments	0	-106	-157	-157
EBITDA	**-2,734**	**-833**	-1,280	-1,365
Operating Profit	-2,787	-914	-1,373	-1,407
Interest income	-32	-16	-3	-3
Profit Before Taxes	**-2,819**	**-930**	-1,376	-1,411
Current tax income	181	174	221	234
Net Income	-2,637	-756	-1,253	-1,176
EPS	-0.57	-0.16	-0.22	-0.19
Balance sheet	**2019**	**2020**	**2021**	**2022e**
Current assets	**347**	**796**	1,823	845
Cash and cash equivalents	4	544	1,670	688
Short-term investments	0	0	0	0
Accounts receivable	163	79	32	32
Inventories	0	0	0	0
Other current assets	180	172	121	124
Non-current assets	**4,288**	**4,331**	4,188	4,146
Property, plant & equipment	28	83	1	1
Intangible assets	4,260	4,248	4,187	4,145
Current liabilities	**-820**	**-347**	-325	-325
Short-term debt	-15	-38	0	0
Accounts payable	-804	-309	-325	-325
Other current liabilities	0	0	0	0
Non-current liabilities	**0**	**-37**	0	0
Long-term debt	0	-37	0	0
Other non-current liabilities	0	0	0	0
Equity	3,815	4,743	4,983	3,964
Share capital	461	490	1,828	1,828
Other	3,355	4,252	3,156	2,136
Cash flow statement	**2019**	**2020**	**2021**	**2022e**
Operating cash flow	-2,251	-718	-1,011	-981
Investing cash flow	-27	-43	44	-1
CAPEX on tangible assets	-27	-43	-1	-1
Financing cash flow	-7	1,301	1,931	0
Proceeds from equity	0	1,338	2,006	0
Net increase in cash	**-2,286**	**539**	963	-981
Cash at start of year	**338**	**4**	543	1,669
Cash at end of year	**4**	**544**	1,669	688
Net cash at end of year	**-11**	**468**	1,670	688

Source: Company; Allenby Capital

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