AozoraStep

Exit PureTech Health: Clinical trial results were not groundbreaking

Company:	PureTech Health (PRTC LN)	**Market Cap:**	$474mio
Industry:	Biotech	**Net Cash:**	$400mio
Country:	USA, UK, global	**Trial success rate:**	>80% (3 FDA approvals)
Date:	20th December 2024	**Cash burn incl. R&D:**	<$130mio p.a.
Dividend:	-	**Programmes in trial:**	17
Entry:	$523mio	**Exit:**	$490mio (-6%)

Why exit PureTech Health?

- LYT-100 (IPF) results did not show significantly lower side effect
- LYT-200 (AML) results showed it could likely end up being used only in combination with other agents for AML
- Expected Seaport's SPT-300 (MDD) phase 2b trial results, instead additional phase 1 study results were published

PureTech after clinical trial results

The position in PureTech Health was always purely event-driven, i.e. results of the trials. With a historic 80% trial success rate, success in either LYT-100 or Seaport Therapeutics SPT-300 phase 2 trials or LYT-200 phase 1 trial appeared almost certain. Overall, the trial results were not negative, but somewhat disappointing.

21 Knightsbridge, London SW1X 7LY
www.aozorastep.com · david@aozorastep.com

LYT-200 phase 1 trial (AML - Acute myeloid leukemia/cancer)

LYT-200's phase 1 trial showed only 59% of the 22 evaluable patients achieving stable disease or better as a single agent[1] compared to currently >50% of AML patients not responding to initial treatment or facing death. Only in combination with other treatments, around 80% of 15 evaluable patients achieved stable or better disease, which is positive, but given the low sample size not groundbreaking.

Seaport's SPT-300 phase 1 trial (MDD - Major depressive disorder/mental health)

I'm not sure whether I made a mistake here or not, but I feel quite confident that their prior presentation talked about SPT-300 phase 2b trial results to be published mid-December. In any case, additional phase 1 trial results were published, which showed that there were no initial side effects from the drug in healthy individuals, but the short duration of somnolence/sleepiness peaking after 4 hours and declining after 6-8 hours only makes it suitable for night use[2]. However, I can imagine that all potential MDD treatments will be focused on sleep. I, as a healthy individual, have tried the medical device from Nexalin[3] that is targeting anxiety and insomnia (could be effective for MDD as well), and got a little sleepy after a few minutes wearing their device. Their CEO also told me that he is using the device before going to bed. SPT-300's phase 2b trial results would need to be groundbreaking given the amount of competition in that newly emerging space.

LYT-100 phase 2 trial (IPF - Idiopathic pulmonary fibrosis/lung disease)

Finally, LYT-100. IPF is a lung disease, which gives patients a 2-5 year life expectancy without treatment. Currently, there are only two treatments on the market: Pirfenidone and Nintedanib. Pirfenidone's main drug is Esbriet and owned by Roche, but their IP has expired, which enabled PureTech to analyse it and modify to come up with LYT-100. It has also led to cheaper products entering the market, leading to a slump in sales for Roche[4]. Nintedanib's main product is OFEV, owned by Boehringer Ingelheim, which

[1] https://news.puretechhealth.com/news-releases/news-release-details/puretech-presents-data-lyt-200-anti-galectin-9-monoclonal
[2] https://news.puretechhealth.com/news-releases/news-release-details/puretech-founded-entity-seaport-therapeutics-presents-additional
[3] https://nexalin.com/
[4] https://www.reuters.com/business/healthcare-pharmaceuticals/roche-explores-selling-lung-disease-drug-bloomberg-reports-2024-02-26/

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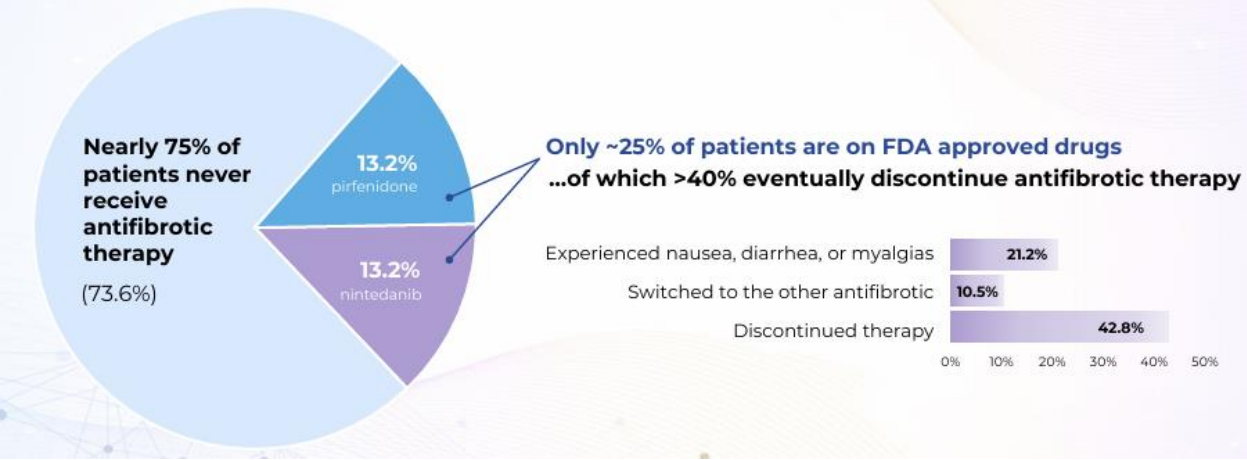
maintains its IP, hence has no cheap competitors and achieved annual sales of €3.5bn last year. Importantly, all products that are on the market only slow down the time to death to around 4.5-7.5 years and have >50% probability of leading to gastrointestinal disorders, i.e. diarrhea, which leads many patients to stop using the treatment and 75% of patients not taking any preventative measures. PureTech Health's mission was especially focused on these 75% of patients not taking the drugs due to side effects. However, the results showed that LYT-100 has a similar degree of side effects as Pirfenidone, but is really on par with OFEV in terms of disease slowdown (OFEV was tested on a 1 year horizon compared to 26 weeks of LYT-100)[5]. But here I made a mistake: I did not know that Boehringer Ingelheim has upcoming phase 3 trial results next year for a new product called BI 1015550, in which a phase 2 trial showed better results of disease slowdown and somewhat fewer side effects in a trial of 48 participants – although the trial was only half the length[6]. Finally, many of the big pharmaceutical companies, such as GSK or Bristol-Myer Squibb are also having trials running on IPF – this sector is very competitive, and the LYT-100 results were positive if released today, but not groundbreaking[7]. In the end, the data was not strong enough to suggest that PureTech could use LYT-100 for the 75% of patients that can't use existing treatments due to side effects.

IPF: Patients often can't stay on current therapy due to side effect



Source: PureTech Health

[5] https://pro.boehringer-ingelheim.com/us/products/ofev/ipf/lung-function
[6] https://www.nejm.org/doi/full/10.1056/NEJMoa2201737?query=featured_home
[7] https://clinicaltrials.gov/search?cond=IPF&aggFilters=status:act%20rec%20not&limit=100&page=1

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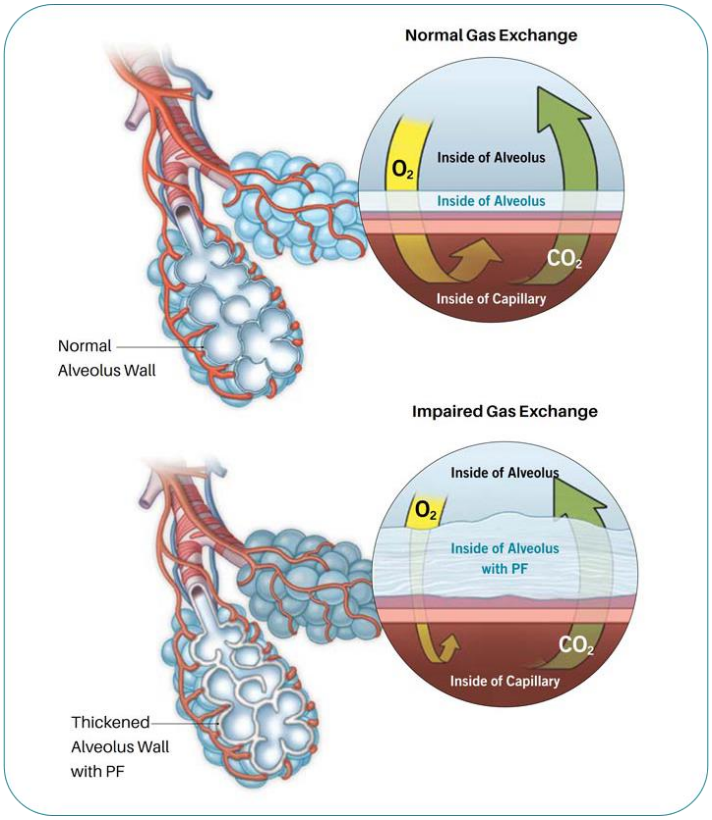
IPF - Idiopathic pulmonary fibrosis



Source: https://www.pulmonaryfibrosis.org/understanding-pff/types-of-pulmonary-fibrosis/idiopathic-pulmonary-fibrosis

LYT-100 phase 2b trial results (26 weeks) vs. OFEV (52 weeks) vs. BI 1015550 (12 weeks)

Agent	Placebo TID (N=65)	Deupirfenidone 550mg TID (N=65)	Deupirfenidone 825mg TID (N=63)	Pirfenidone 801mg TID (N=61)	OFEV INPULSIS after 1 year (N=307)	OFEV TOMORROW after 1 year 150mg TID (N=86)	BI 1015550 (N=97)	Placebo in BI 1015550 trial (N=50)
Forced Vital Capacity mL change after 26 weeks/52wks/12wks	-112.5	-80.7	-21.5	-51.6	-95	-50	4.2	-59.2

Source: https://investors.puretechhealth.com/static-files/f0d99386-1d67-4359-911d-468ceeb84594, https://pro.boehringer-ingelheim.com/us/products/ofev/ipf/lung-function, https://www.nejm.org/doi/full/10.1056/NEJMoa2201737?query=featured_home

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LYT-100 phase 2b trial results

Agent	Placebo TID (N=65)	Deupirfenidone 550mg TID (N=65)	Deupirfenidone 825mg TID (N=63)	Pirfenidone 801mg TID (N=61)
Forced Vital Capacity pp change after 26 weeks	-3.43	-1.81	-0.43	-1.46

Source: https://investors.puretechhealth.com/static-files/f0d99386-1d67-4359-911d-468ceeb84594

LYT-100 phase 2b trial results vs. OFEV vs. BI 1015550

SOC/PT	Placebo TID (N=65) n (%)	Pirfenidone 801mg TID (N=61) n (%)	Deupirfenidone 550mg TID (N=65) n (%)	Deupirfenidone 825mg TID (N=63) n (%)	OFEV after 1 year (N=307)	BI 1015550 18mg TDI (N=97)
Gastrointestinal disorders	16 (24.6)	33 (52.4)	23 (35.4)	34 (53.1)	190 (62)	
Nausea	5 (7.7)	17 (27)	11 (16.9)	13 (20.3)		
Dyspepsia	2 (3.1)	14 (22.2)	8 (12.3)	9 (14.1)		
Diarrhea	6 (9.2)	7 (11.1)	7 (10.8)	5 (7.8)		8 (17)
Abdominal pain	3 (4.6)	5 (7.9)	4 (6.2)	9 (14.1)		
Constipation	1 (1.5)	4 (6.3)	1 (1.5)	3 (4.7)		
Vomiting	0 (0)	2 (3.2)	5 (7.7)	1 (1.6)		

Source: https://investors.puretechhealth.com/static-files/f0d99386-1d67-4359-911d-468ceeb84594, https://pro.boehringer-ingelheim.com/us/products/ofev/ipf/lung-function, https://www.nejm.org/doi/full/10.1056/NEJMoa2201737?query=featured_home

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