VALUATIONLAB
FINANCIAL ANALYSIS

SPEXIS

FOCUS AREA: RARE CHRONIC RESPIRATORY DISEASES AND TREATMENT-RESISTANT CANCER

KEY DATA			SIX: SPEX
MARKET CAPITALIZATION (CHF MN)	40	**SHARE PRICE ON 17 AUGUST 2022**	0.8
ENTERPRISE VALUE (CHF MN)	25	**RISK-ADJUSTED NPV PER SHARE** * (CHF)	3.6
CASH (31 DECEMBER 2021) (CHF MN)	14	**UPSIDE/DOWNSIDE** (%)	335%
MONTHLY OPERATING EXPENSE (CHF MN)	1.2	**RISK PROFILE**	SPECULATIVE
CASH LIFE		**SUCCESS PROBABILITY LEAD PROJECT**	55%
BREAK-EVEN (YEAR)		**EMPLOYEES**	30
FOUNDED (YEAR)	2021	**LISTED** (YEAR)	2018

KEY PRODUCTS:	STATUS	MAJOR SHAREHOLDERS:	(%)
- COLIFIN (CYSTIC FIBROSIS P. AERUGINOSA)	PHASE III / LAUNCHED (EU)	- RLG BUSINESS CORPORATION	12.8
- INHALED MUREPAVADIN (CYSTIC FIBROSIS P. AERUGINOSA)	PHASE I	- VECTURA GROUP LIMITED	9.0
- BALIXAFORTIDE (CANCER, OTHER INDICATIONS TBD)	PHASE II	- INGRO FINANZ AG	<5.0
- NEW CXCR4 INHIBITOR (E.G. BLOOD CANCERS)	PRECLINICAL	- EXECUTIVE MANAGEMENT	20.5
- LONODELESTAT (CYSTIC FIBROSIS) - SANTHERA ROYALTIES	PHASE I	**- FREE FLOAT**	80
		- AVERAGE DAILY VOLUME (3-MONTHS)	9,958

UPCOMING CATALYSTS:	DATE	ANALYST(S):	BOB POOLER
- BALIXAFORTIDE (E.G. BLOOD CANCERS) - STRATEGIC DECISION	H2 2022		BP@VALUATIONLAB.COM
- COLIFIN (CYSTIC FIBROSIS) - START US "COPILOT" DOSING TRIAL	H1 2023		+41 79 652 67 68
- COLIFIN (CYSTIC FIBROSIS) - START US "COPA" PHASE III TRIAL	H2 2023		

* NOTE: 158.1 MN SHARES USED FOR CALCULATION OF RISK-ADJUSTED NPV/SHARE, ASSUMING ADDITIONAL CHF 90 MN NEEDED TO LAUNCH COLIFIN IN THE US

ESTIMATES AS OF 17 AUG 2022

SOURCE: SPEXIS, VALUATIONLAB ESTIMATES

Catching breath in lung disease

ColiFin US phase III CF trial to start in H1 2023

Spexis AG, formed from the reverse merger of EnBiotix into Polyphor, resulting in EnBiotix shareholders holding ~75% of Spexis' outstanding shares, is focused on discovering, developing, in-licensing, and acquiring first-in-class or best-in-class drugs for rare diseases and cancer. The initial rare disease focus is on chronic respiratory disease with the aim to become an important player in the market for chronic lung infections in cystic fibrosis with ColiFin (phase III-ready), and inhaled murepavadin (phase I). Spexis in-licensed the global rights (excluding Europe) of ColiFin from PARI Pharma, which sells ColiFin in Europe, to develop and commercialize ColiFin in the lucrative US market. The ColiFin single pivotal phase III program (COPILOT + COPA) should start in H1 2023. In cancer, the initial focus will be on novel CXCR4/CXCR7 inhibitors, including balixafortide, with a strategic decision to be made in H2 2022 on whether and how to further develop balixafortide after the negative phase III readout in advanced triple-negative metastatic breast cancer in June 2021. With a cash reach until the end of January 2023 (excluding a potential extension through the IRIS line) Spexis is seeking strategic transactions and financings to replenish its cash position. We calculate CHF ~90 mn will be needed to fully develop and commercialize ColiFin in the US market. We derive a sum-of-parts risk-adjusted (r)NPV of CHF 3.6/share, conservatively accounting for 158.1 mn shares to raise CHF 90 mn at the current low share price. We qualify Spexis as Speculative with the need to secure near-term and sufficient funding.

Key catalysts:

1) **Strategic decision balixafortide (H2 2022):** to move forward on solid tumors and/or other indications.
2) **Start of ColiFin "COPILOT" dosing trial in cystic fibrosis (H1 2023):** to determine if ColiFin can be given once-daily, providing a substantial competitive advantage; topline results due in H2 2023.
3) **Start of ColiFin single pivotal US phase III "COPA" trial in cystic fibrosis (H2 2023):** required to gain approval in the lucrative US market with topline results due in mid-2025; US peak sales could amount to CHF 300+ mn.

Strategy & Cash Position

Swiss biopharma company focused on rare, chronic respiratory diseases and cancer
Spexis AG (derived from the Latin "spes" which means hope) is a clinical-stage biopharmaceutical company formed as the result of the reverse merger of the Allschwil (near Basel), Switzerland-based Polyphor AG (founded in 1996), and the Boston, US-based, EnBiotix Inc. (launched in 2012), which was finalized in December 2021. The company is headquartered in the BioPharma Cluster Basel in Allschwil, Switzerland with a staff of approximately 30 employees, and is listed on the SIX Swiss Stock Exchange (ticker: SPEX.SW). Spexis is focused on discovering, developing, in-licensing, and acquiring first-in-class or best-in-class compounds for rare diseases and cancer. All of the company's products are derived from its proprietary macrocycle-based discovery platform with the exception of ColiFin (inhaled colistimethate sodium or colistin, and which is also a macrocycle), where the worldwide rights, excluding Europe, were in-licensed from PARI Pharma.

Spexis has an initial focus on two therapeutic areas:

1) **Rare, chronic respiratory diseases:** Spexis's current rare disease focus is on rare, chronic respiratory diseases in general, and in particular, to become an important player in the management of chronic lung infections in cystic fibrosis, where current therapies are increasingly inadequate due to decreased efficacy over time, significant toxicities and increasing antimicrobial resistance. Spexis's lead compounds targeting chronic lung infections include:
    - **ColiFin** (branded inhaled colistin formulation) marketed in Europe, US phase III-ready) for treating *Pseudomonas aeruginosa* (*P. aeruginosa*) infections in patients with cystic fibrosis, the leading cause of exacerbations, lung function decline, and death; global rights, excluding Europe, has been in-licensed by Spexis from PARI Pharma that sells ColiFin in a handful of European countries; ColiFin is phase III-ready in the US where a single phase III trial is required for approval; the start of the "COPILOT" dosing trial to determine if ColiFin can be given once-daily in H1 2023 with topline results due in H2 2023; the US phase III "COPA" trial is planned to start in H2 2023 with topline results due in mid-2025; we forecast peak sales to amount to CHF 300+ mn. Positive interim analysis results (late 2024/early 2025) could lead to accelerated US approval by roughly one year in mid-2025 instead of H1 2026.
    - **Inhaled murepavadin** (phase I) for treating *P. aeruginosa* infections in patients with cystic fibrosis; preclinical development completed suggesting broad safety margin and efficacy, CTA (clinical trial application) granted in December 2020, a safety and tolerability trial completed Part A (healthy volunteers) with Part B (cystic fibrosis patients) planned to start by end of 2022; largely financed by the EU IMI (Innovative Medicines Initiative) program and Cystic Fibrosis Foundation; phase Ib/IIa proof-of-concept (POC) development expected to be initiated in 2023 (dependent on sufficient funding); peak sales in cystic fibrosis alone could amount to CHF 200 - 400 mn (comparator peak sales); a potential expansion into larger indications such as non-cystic fibrosis bronchiectasis (nCFBE).
    - **Lonodelestat** (phase I – global rights licensed to Santhera) for the treatment of cystic fibrosis and other neutrophilic lung diseases; global rights licensed to

Santhera in 2018; positive topline results of the multiple ascending dose (MAD) phase Ib trial in cystic fibrosis reported in March 2021; Spexis is eligible of up to CHF 121 mn in milestones and tiered double-digit royalties on sales; potential in other lung disorders associated with high human neutrophil elastase (hNE) activity including, ARDS (acute respiratory distress syndrome), AAT (alpha-1 antitrypsin deficiency) and nCFBE (non-cystic fibrosis bronchiectasis).

2) **Oncology:** Spexis's current focus in cancer is on CXCR4/CXCR7 active compounds discovered and developed by applying the company's leading macrocycle technology platform. Spexis's key oncology compound is:
    - **Balixafortide** (strategic decision for other possible indications H2 2022) Spexis is currently evaluating how to further develop balixafortide, its novel immuno-oncology CXCR4 compound, after the negative outcomes from the pivotal "FORTRESS" phase III trial in advanced HER2 negative locally recurrent or metastatic breast cancer, Spexis is considering other clinical and preclinical data supporting a variety of additional oncology and rare disease indications
    - **New CXCR4 lead compound** (preclinical) a potent, highly selective CXCR4 inhibitor was identified based on the company's macrocycle platform technology platform; targets hematological malignancies (blood cancers) such as lymphoma, leukemia, and myeloma, a sizable untapped market; patent application to be filed in H2 2022 and shortly thereafter the new compound is expected to be disclosed with its first lead indication(s)

The main objective is to build a leading company in rare diseases and cancer

Spexis's main objective is to build a leading biopharmaceutical company discovering, developing, in-licensing, and acquiring innovative compounds and programs focused on rare diseases and cancer. The company's strategy is to create value by building a comprehensive portfolio of first-in-class or best-in-class compounds for rare respiratory diseases and cancer based on its proprietary macrocycle drug discovery platform Spexis plans to develop these compounds up to important value inflection points such as POC, phase III, or market approval, and then either out-license the commercialization rights to a major pharmaceutical company, or, where attractive, establish its own specialist sales force to retain and maximize value. Its commercial strategy will be influenced by addressable patient populations, the degree of unmet medical need, and the pricing and reimbursement practices of different countries, among other factors.

Spexis's key priorities for the next 12-18 months include:

1. **Chronic respiratory disease (CRD):**
    - Start of the ColiFin "COPILOT" once- vs. twice-daily dosing phase III pilot trial to evaluate a potential USP once-daily dosing of ColiFin in cystic fibrosis in Q1 2023; topline results are due in H2 2023
    - Start the single pivotal phase III "COPA" trial required for US approval of ColiFin in cystic fibrosis in H2 2023; topline results due in mid-2025
    - Complete Part B of its phase Ia safety and tolerability trial of inhaled murepavadin in cystic fibrosis with topline results expected in Q4 2022 and initiate Part C in patients with cystic fibrosis.

2. **Oncology:**
   - Complete the balixafortide analyses for possible future clinical trials in cancer or non-oncology indications
   - Identify additional novel development candidates in the field of immuno-oncology based on the proprietary macrocycle technology platform

3. **Business development / strategic transactions:**
   - Pursue additional partnerships and/or financings in 2022 and 2023 to support and finance the company's clinical development plans for ColiFin and inhaled murepavadin in cystic fibrosis
   - Pursue application of and partnerships relating to the macrocycle platform in the areas of molecular glues, protein degraders and other applications
   - Consider strategic transactions targeting mid or late clinical-stage products

More than CHF 400 mn raised since its foundation in 1996

The company has been successful in raising money. Since its foundation in 1996 and prior to the IPO in 2018, the company raised approximately CHF 210 mn from a Swiss and international investor base, including Ingro Finanz, Varuma, BioMed Partners, and Rosetta Capital. In addition, several of the company's development programs have benefitted or still benefit from funding or other financial support provided by Eurostars, CTI (Commission for Technology and Innovation; now Innosuisse), The Cystic Fibrosis Foundation (CFF), the Wellcome Trust Limited, the Innovative Medicines Initiative (IMI) and CARB-X (Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator), among others.

MONEY RAISED	CHF MN
PRE-IPO	210
IPO (INITIAL PUBLIC OFFERING)	165
CONVERTIBLE BONDS	19
TOTAL RAISED	**406**

SOURCE: SPEXIS, VALUATIONLAB

CHF 165 mn was raised during the IPO in May 2018, becoming the largest biotech IPO in Switzerland since 2009 and one of the top three in Europe since 2016 in terms of proceeds raised by an issuer to finance the development of its pipeline. In July 2020, the company entered into an equity-linked financing agreement with the French company IRIS, where it can raise a gross amount of up to CHF 19.3 mn over a period of two years. IRIS will receive Spexis shares to be created from the company's conditional capital based on the interest-free mandatory convertible bonds program. IRIS is committed to buying on a monthly basis over a period of two years twenty-four tranches of CHF 800,000 of unsecured zero-coupon mandatory convertible bonds. The program can be tailor-made in terms of period and tranche size, according to Spexis' financing needs, while the company may suspend or terminate the staggered financing. During the term of the financing, IRIS will convert each month the mandatory convertible bonds into shares at a discount to the applicable volume-weighted average price (VWAP). These shares are expected to be sold on the market or in block trades.

In December 2021, prior to the closing of the reverse merger of Polyphor and EnBiotix into Spexis, EnBiotix closed a USD 12.8 mn, pre-merger, round of financing with Vectura Group plc (USD 7.6 mn), the Cystic Fibrosis Foundation (USD 2.4 mn), Sanford Biosciences LLC

(USD 1 mn) and others. The financing was led by Vectura, a leader in inhaled therapeutics, which is currently wholly owned by Philip Morris International (PMI).

Additional funding is required to finance ColiFin US approval and commercialization
To finance ColiFin up to full development and US commercialization in cystic fibrosis and inhaled murepavadin up to proof-of-concept (POC) in cystic fibrosis, we calculate Spexis will need additional funding of approximately CHF 90 mn, which can be raised in several financing rounds at various value inflection points to minimize share dilution, as well as through non-equity-based funding.

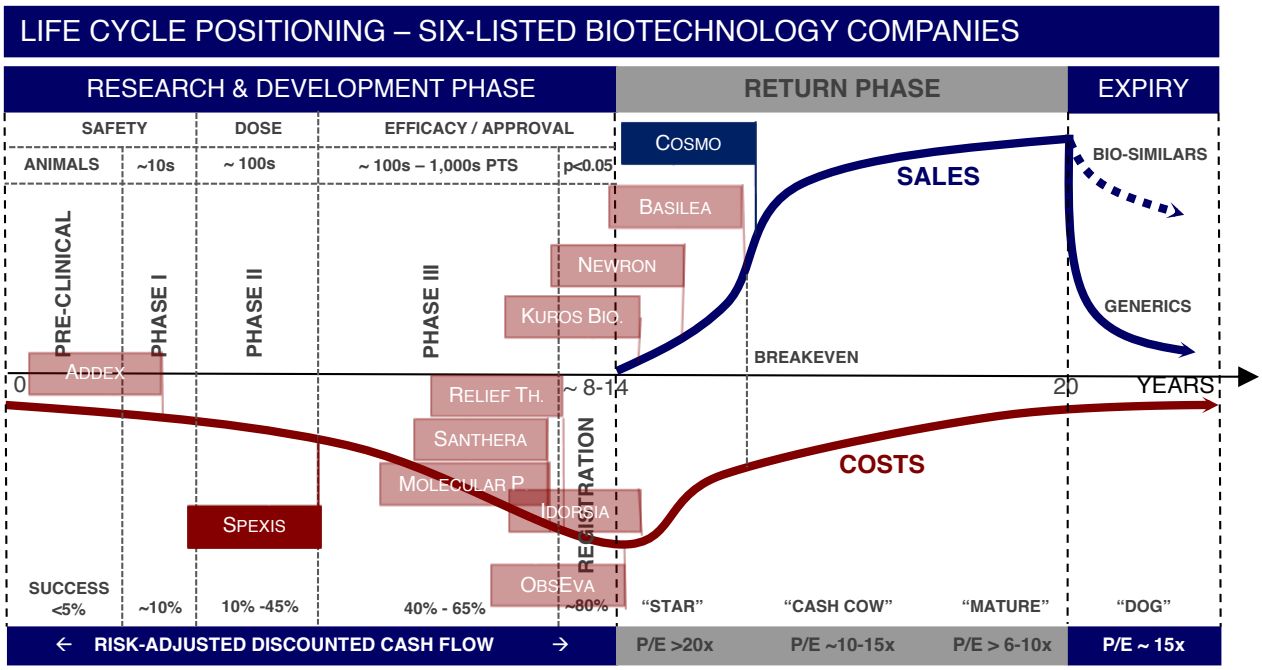
With cash and cash equivalents of CHF 14.4 mn (31 December 2021), and up to USD 19.5 mn grants awarded from CARB-X and the Cystic Fibrosis Foundation, Spexis expects to have sufficient funds for operations until the end of January 2023. The equity-linked financing by IRIS can extend the company's cash life if needed. The start of the ColiFin "COPILOT" dosing trial to assess the potential of once-daily dosing is planned to start in H1 2023 with results due in H2 2023. Positive results provide ColiFin with an additional unique selling point of once-daily dosing, while competitor products require at least twice-daily dosing with a cumbersome nebulizer. We expect Spexis to raise capital in several rounds in the financial markets on reaching certain value inflection points such as the start of the "COPILOT" dosing trial, the start of the "COPA" trial, or the release of positive results of these trials, at a considerably higher share price than the current depressed valuation (caused by the discontinuation of lead compound balixafortide in advanced breast cancer in May 2021) to minimize share dilution.

Important to note is that ColiFin is already approved in the EU and has become a front-line treatment for cystic fibrosis. Hence, we believe the development risk is relatively low compared to our conservative 55% (phase III-ready) success rate.

To account for the funding gap, which will likely be realized in multiple steps on reaching various value inflection points, we conservatively calculate our per share forecasts based on 158.1 mn shares (48.3 mn shares outstanding plus an estimated 109.8 mn new shares) to raise the estimated CHF 90 mn capital needed to fully develop and start the US commercialization of lead compound ColiFin in cystic fibrosis with estimated peak sales of CHF 300+ mn. This leads to a 227% share dilution based on the current depressed share price level. Note that Spexis plans to raise the required funds in several funding rounds on reaching certain value inflection points as mentioned above. This should lead to a considerably lower share dilution than we conservatively base our sum-of-parts rNPV for Spexis at the moment. Spexis also has other options to secure additional financing, which besides equity-based funding also includes debt financing, royalty financing, or monetizing assets such as ColiFin regional rights.

Life Cycle Positioning – Speculative

We qualify Spexis' risk profile as Speculative with currently no revenues and a limited cash reach until the end of January 2023 with a potential extension through the IRIS line. The company will need to replenish its cash position in a timely manner to finance its growth plans. 2023 should provide several value inflection points, including the start (Q1) and results (H2) of the "COPILOT" once-daily (QD) vs. twice-daily (BID) dosing trial of ColiFin in cystic fibrosis (potential USP of once-daily dosing); the start of the single phase III "COPA" trial (H2) required for US approval of ColiFin in cystic fibrosis. Topline results of the phase I (parts A and B) safety trial of inhaled murepavadin (Q4 2022) in cystic fibrosis, with the compound expected to move to phase Ib/IIa POC (part C) development (2023) partially funded by the IMI and upon securing sufficient additional funding. Moreover, a strategic decision regarding balixafortide potentially in other cancer indications or non-cancer indications will be made in H2 2022 (see Important Disclosures for our Risk Qualification).



SOURCE: VALUATIONLAB

Valuation Overview

Risk-adjusted sum-of-parts NPV points to a fair value of CHF 3.6 per share
We derive a sum-of-parts risk-adjusted NPV of CHF 3.6 per share for Spexis, conservatively based on a share dilution of 227% (158.1 mn shares) based on the currently depressed market capitalization to raise around CHF 90 mn to fully fund ColiFin up to profitability, with cash of CHF 0.1 per share (31 December 2021) and overhead expenses of CHF 0.2 per share, assuming a WACC of 7% (reflecting the low Swiss interest environment).

SUM OF PARTS

PRODUCT	INDICATION	PEAK SALES (CHF MN)	LAUNCH YEAR (EST)	UNADJUSTED NPV/SHARE * (CHF)	SUCCESS PROBABILITY	RNPV/SHARE * (CHF)	PERCENTAGE OF TOTAL
COLIFIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTIONS	344	2025	6.7	55%	**3.7**	98%
MUREPAVADIN (INHALED)	CYSTIC FIBROSIS P. AERUGINOSA INFECTIONS	193	2028	2.0			
BALIXAFORTIDE	CANCER, OTHER INDICATIONS TBD	TBD	TBD	TBD			
NEW CXCR4 CANDIDATE	BLOOD CANCERS	TBD	TBD	TBD			
LONODELESTAT (SANTHERA ROYALTIES)	CYSTIC FIBROSIS	964	>2025	1.0			
CASH POSITION (31 DECEMBER 2021)		14.4		0.1		**0.1**	2%
TOTAL ASSETS				3.1		**3.8**	100%
OVERHEAD EXPENSES				-0.2		**-0.2**	
NPV/SHARE (CHF)				2.9		**3.6**	
SHARE PRICE ON 17 AUGUST 2022						0.8	
PERCENTAGE UPSIDE / (DOWNSIDE)						335%	

* NOTE: 158.1 MN SHARES USED FOR CALCULATION OF RISK-ADJUSTED NPV/SHARE, ASSUMING ADDITIONAL CHF 90 MN NEEDED TO LAUNCH COLIFIN IN THE US

ESTIMATES AS OF 17 AUG 2022 SOURCE: VALUATIONLAB ESTIMATES

Spexis' key driver is currently limited to:

ColiFin in cystic fibrosis - rNPV of CHF 3.7 per share
We forecast US peak sales of ColiFin in cystic fibrosis to amount to CHF 300+ mn. Spexis acquired global rights (excluding Europe) from PARI Pharma. ColiFin has been approved in the EU since 2010 and is front-line therapy for cystic fibrosis. In the US, where intravenously administered colistin is approved for systemic use in acute infections, the intravenous formulation is prescribed "off-label" (not approved by the FDA and prescribed only at the instigation of the physician) for inhalation in cystic fibrosis patients. Inhaled colistin is prescribed off-label to approximately 36% of adult cystic fibrosis patients with moderate to severe lung disease and who do not respond or tolerate currently approved cystic fibrosis treatments in the US. Approved drugs in the US receive formal pricing and reimbursement for treatment of the indication, while the physician is potentially liable for prescribing a medication for a non-approved indication. This provides a unique opportunity for Spexis to seek official FDA approval in the US. The FDA requires only a single phase III trial for ColiFin to acquire US approval in cystic fibrosis.

Spexis plans to start the "COPILOT" once-daily (QD) vs. twice-daily (BID) dosing trial in H1 2023 with results in H2 2023 to assess whether ColiFin can be given once daily, potentially providing an additional USP compared to competitor drugs, which have to be given at least twice daily with a nebulizer. In H2 2023, the phase III "COPA" trial is expected to start with topline results due in mid 2025 with the NDA (new drug application) submission planned for H2 2025. Assuming Priority Review (6-months instead of 10-months) review, based on Fast Track designation received in November 2020, ColiFin could be approved and launched in the US by H1 2026. Spexis plans to build its own small specialist sales force of approximately 20 FTEs to market ColiFin in the US to retain and maximize long-term value. Its specialist sales force could be leveraged to market inhaled murepavadin if successfully developed and approved for cystic fibrosis.

The US market provides a unique "switch" opportunity for ColiFin with an estimated 36% of adult patients with moderate or advanced disease currently treated with off-label colistin. We forecast peak sales in this immediately capturable market of roughly 3,500 patients to amount to approximately CHF 150 mn, with a rapid market penetration reaching 90% in just a few years. For other patients (not treated with colistin), we forecast a gradual uptake and lower peak market penetration of ~30% in patients with advanced disease and ~15% in patients with moderate disease, with peak sales for this patient group amounting to approximately CHF 200 mn. In March 2020, ColiFin was granted Orphan Drug designation, which provides an additional 7 years of market exclusivity on top of 5 years of Qualified Infectious Disease Product (QIDP) exclusivity for a total of 12 years from FDA approval. We calculate an rNPV of CHF 584 mn or CHF 3.7/share for ColiFin in cystic fibrosis, with a 55% (phase III-ready) success probability and a WACC of 7%.

NOTE: Positive interim analysis results of the "COPA" trial planned for late 2024/early 2025 could potentially lead to accelerated US approval by roughly one year in mid-2025. Our success probability will increase to a historical 65% phase III rate upon the start of the phase III "COPA" trial in H2 2023, which can be considered conservative, as ColiFin is already approved in the EU and generic colistin is prescribed off-label in the US.

Currently, no value attributed to early-stage pipeline projects

We have conservatively not accounted for Spexis's early-stage pipeline projects due to the lack of sufficient proof-of-concept at the moment. Spexis's unadjusted NPV provides a "sneak preview" of what the value could amount to if all our assumptions were reached.

Inhaled murepavadin *P. aeruginosa* in cystic fibrosis – Phase I, launch 2028E

Inhaled murepavadin is also targeted to treat *P. aeruginosa* infections in cystic fibrosis. The compound was discovered and developed entirely in-house via the company's proprietary platform and has completed preclinical development and received a clinical trial application (CTA) in the UK in December 2020. Phase I development in human volunteers started in Q4 2021 with the topline results expected in Q4 2022 and results in cystic fibrosis patients (Part C) expected in mid-2023. A phase IIa proof-of-concept (POC) trial in cystic fibrosis patients is expected to start in late 2023. Inhaled murepavadin has the potential for Orphan Drug Designation (ODD), providing 7 years (US) and 10 years (EU) market exclusivity from approval. Peak sales could amount to CHF 200 – 400 mn (based on comparator drugs).

Lonodelestat in cystic fibrosis (out-licensed to Santhera) – Phase I, launch >2025

In February 2018, the exclusive global rights for lonodelestat were licensed to Santhera. Spexis is entitled to up to CHF 121 mn in regulatory, development, and sales milestones and tiered royalties up to 10% on lonodelestat sales. Lonodelestat is a novel, selective human neutrophil elastase (hNE) inhibitor for treating cystic fibrosis and other rare lung disorders. In early March 2021, positive phase Ib multiple ascending dose (MAD) trial results in cystic fibrosis patients were reported with POC development potentially to start in 2022 (dependent on Santhera securing sufficient funding). Assuming lonodelestat captures a conservative 15% of the market with a USD 70,000 to USD 100,000 annual treatment price, peak sales could potentially amount to around CHF 1 bn for cystic fibrosis alone. Additionally, imbalanced neutrophil activity is associated with a large number of inflammatory diseases, which could add to the market potential such as AAT (alpha-1 antitrypsin deficiency) and nCFBE (non-cystic fibrosis bronchiectasis).

Balixafortide in new indications & combinations – Preclinical, launch TBD
Following the negative "FORTRESS" ORR results in Q2 2021, Spexis is evaluating the use in other cancer indications or non-oncology indications. CXCR4 expression has been validated as a negative prognostic factor for at least 23 cancer types other than breast cancer. A strategic decision is expected in H2 2022.

New CXCR4 lead compound in blood cancers – Preclinical, launch TBD
A patent application will be filed for the new CXCR4 lead compound in H2 2022 and shortly thereafter the compound and its first lead indication(s) are expected to be disclosed. We will include forecasts for the new CXCR4 lead compound once the lead indication has been determined and the compound starts POC development.

Sensitivities that can influence our valuation

Funding risk: With cash of CHF 14 mn (31 December 2021), Spexis can fund operations until the end of January 2023. The equity-linked financing agreement by IRIS could extend cash life if needed. We calculate Spexis will need additional funding of around CHF 90 mn to fully develop ColiFin in cystic fibrosis and build its own small specialist sales force to commercialize the drug and retain and maximize the long-term value in the lucrative US market and develop inhaled murepavadin up to proof-of-concept (POC).

Development risk: ColiFin is a relatively low-risk late-stage development compound that is already approved as a front-line treatment for cystic fibrosis in the EU since 2010. The US FDA requires only a single pivotal phase III trial for US approval in cystic fibrosis, and Spexis has already received an FDA "Study May Proceed" letter. We conservatively apply a 55% (phase III-ready) success rate that will increase to a historic 65% success probability once the "COPA" trial starts in H2 2023. Inhaled murepavadin is in early phase I safety development with no POC in cystic fibrosis, while Spexis's novel new CXCR4 lead compound is still in preclinical development where historical success rates are typically lower than 5% and therefore not included in our forecasts, yet.

Commercialization risk: Spexis does not have its own sales organization to commercialize ColiFin in the US. Following positive "COPA" results, the company plans to build its own small specialist sales force of around 20 FTEs to commercialize ColiFin and potentially inhaled murepavadin in the US. Market penetration and sales uptake could be lower than our forecasts, dependent on the success and marketing muscle of Spexis's US sales force.

Pricing and reimbursement risk: US approval of ColiFin leads to formal pricing and reimbursement in cystic fibrosis. Spexis is targeting to price ColiFin around the middle of the pricing range of generic and branded inhaled antibacterials used chronically for cystic fibrosis. ColiFin is expected to rapidly replace generic off-label colistin, while a potentially superior profile at lower pricing than branded drugs should lead to faster and higher market penetration in other patients. Pricing could be lower, and reimbursement negotiations could take longer than forecast.

Manufacturing risk: Spexis does not have any manufacturing facilities nor has plans to establish these. The company will continue to rely on third-party contract manufacturers for preclinical and clinical testing.

Intellectual property risk: ColiFin should enjoy at least 12 years of market exclusivity in the US, consisting of 5 years of Qualified Infectious Disease Product (QIDP) and 7 years of Orphan Drug market exclusivity from FDA approval. Spexis' macrocycle platforms PEMfinder and MacroFinder have resulted in 47 patent families with more than 500 patents and patent applications in over 50 countries, which are directed to compounds, formulations, processes and uses. Inhaled murepavadin should enjoy market exclusivity throughout 2036 through the composition of matter (COM) patent, additional IP, and potential QIDP and Orphan Drug market exclusivity. Balixafortide is protected by 10 patent families related to CXCR4 antagonists. Its COM patent (WO2008/104090) expires in 2027 (EP) and 2028 (US) but is eligible for patent term extensions of up to 5 years in the EU by SPC (Supplementary Protection Certificate) and the US by PTE (Patent Term extension). In addition, a number of patent strategies for balixafortide to expand its patent life are being developed.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE / EVENT	COMMENT	IMPACT ON RNPV
2022					
3 MAR			CARB-X MILESTONE	SECOND PART OF PHASED FUNDING GRANT FROM CARB-X AWARDED TO SUPPORT THE CONTINUATION OF THE THANATIN DERIVATIVES PROGRAM; CARB-X TO PROVIDE UP TO USD 1.9 MN TO INITIATE LEAD OPTIMIZATION; ELIGIBLE UP TO USD 8.84 MN ADDITIONAL FUNDS TO NOMINATE A PRECLINICAL CANDIDATE	
24 MAR			FY 2021 RESULTS & BUSINESS UPDATE		
26 APR			AGM	ALL AGENDA ITEMS APPROVED INCLUDING THE MEMBERS OF BOARD WERE RE-ELECTED, AND INCREASES IN AUTHORIZED AND CONDITIONAL CAPITAL, AMONG OTHERS	
6 SEP				H1 2022 RESULTS	
H2	BALIXAFORTIDE	SOLID TUMORS	STRATEGIC DECISION	STRATEGIC DECISION TO MOVE FORWARD ON SOLID TUMORS AND/OR OTHER INDICATIONS	
H2	COLIFIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	"COPILOT" DOSING TRIAL - PREPARATION	PREPARATION OF THE "COPILOT" DOSING TRIAL	
H2	SPX-001, SPX-002, CXCR4 INHIBITORS			EVALUATE SPX-001, SPX-002 AND CXCR4 INHIBITORS FOR POSSIBLE FURTHER CLINICAL DEVELOPMENT IN RARE CHRONIC RESPIRATORY DISEASES	
H2	NEW CXCR4 INHIBITOR	HEMATOLOGICAL MALIGNANCIES	DETERMINE TARGET INDICATION(S)	NOMINATE HEMATOLOGICAL CANCER INDICATION(S) BASED ON PRECLINICAL PROOF-OF-CONCEPT (POC) DATA OVERCOMING RESISTANCE OF STANDARD OF CARE (SOC)	
H2			STRATEGIC TRANSACTIONS CLINICAL PIPELINE	PURSUE STRATEGIC TRANSACTIONS TARGETING MID/LATE CLINICAL STAGE PRODUCTS	
H2			ADDITIONAL PARTNERSHIPS/FINANCINGS	PURSUE ADDITIONAL PARTNERSHIPS/FINANCINGS IN 2022 AND 2023 TO SUPPORT SPEXIS' CLINICAL DEVELOPMENT PLANS	
Q4	INHALED MUREPAVADIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	PHASE IA - TOPLINE RESULTS	TOPLINE RESULTS OF PHASE IA SAFETY TRIAL WHICH STARTED IN Q4 2021; SUPPORTED BY BOTH THE IMI (INNOVATIVE MEDICINES INITIATIVE) AND CFF (CYSTIC FIBROSIS FOUNDATION)	
2023					
H1	COLIFIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	"COPILOT" DOSING TRIAL - START	START OF THE "COPILOT" DOSING TRIAL IN 38 PATIENTS EQUALLY RANDOMIZED TO 19 PATIENTS 2X DAILY DOSING AND 19 PATIENTS 1X DAILY DOSING OF COLIFIN FOR 28-DAYS TO DETERMINE IF COLIFIN CAN BE GIVEN ONCE-DAILY IN THE PHASE III "COPA" TRIAL, WHICH WOULD BE A COMPETITIVE ADVANTAGE; IN-MARKET TREATMENTS REQUIRE 2X OR 3X DAILY DOSING	
	INHALED MUREPAVADIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	PHASE IB/IIA POC TRIAL - START	START OF PHASE IB/IIA PROOF-OF-CONCEPT (POC) TRIAL (DEPENDENT ON SECURING FUNDING)	
H2	COLIFIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	"COPILOT" DOSING TRIAL - READ OUT	READOUT OF THE "COPILOT" TRIAL AFTER LAST PATIENT OUT TO DETERMINE IF COLIFIN CAN BE GIVEN 1X DAILY IN THE PHASE III "COPA" TRIAL	
H2	COLIFIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	"COPA" PHASE III TRIAL - START	START OF THE PHASE III "COPA" TRIAL WITH THE FIRST PATIENT ENTERING THE CLINIC	+CHF 0.7
Q4	INHALED MUREPAVADIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	PHASE IB/IIA - TOPLINE RESULTS	TOPLINE RESULTS PHASE IB/IIA POC TRIAL	
2024					
H1	INHALED MUREPAVADIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	PHASE IIB/III TRIAL - START	START PHASE IIB/III DOSE-RANGING TRIAL	
LATE	COLIFIN	CYSTIC FIBROSIS P. AERUGINOSA INFECTION	"COPA" PHASE III TRIAL - INTERIM ANALYSIS	INTERIM EFFICACY ANALYSIS SCHEDULED AFTER 60% OF PATIENTS HAVE COMPLETED 28 DAYS TREATMENT; POTENTIAL OF ACCELERATED APPROVAL IN THE US BY APPROXIMATELY ONE YEAR IN 2025 INSTEAD OF OUR BASE CASE OF MID-2026	

ESTIMATES AS OF 17 AUG 2022

SOURCE: SPEXIS, VALUATIONLAB ESTIMATES

Technology & Pipeline

Proprietary macrocycle platform applicable to many therapeutic areas & targets
Quite remarkable for a company of its size, Spexis has a proprietary macrocycle-based drug discovery platform applicable to many therapeutic areas and targets. Except for lead compound ColiFin, which global rights (excluding Europe) were in-licensed from PARI Pharma, all of the company's compounds originate from its own discovery platform.

Macrocycle-based discovery platform
The macrocycle-based discovery platform is the result of over 25 years of research, several historical drug discovery service-type partnerships, and more than USD 400 investment. Both balixafortide and murepavadin and several other undisclosed drug development candidates have been derived from this platform. In addition, ColiFin is also a macrocycle compound, although in-licensed from PARI Pharma and not discovered in-house.

The macrocycle-based drug discovery platform is based on two complementary technologies:

- **PEMfinder:** Protein Epitope Mimetics (PEM) are conformationally constrained cyclopeptides mimicking the biologically most relevant protein surface epitopes such as the β-hairpin and α-helix motifs. PEMfinder is a highly diverse library derived from sequences of many bioactive peptides including peptide hormones, ligands of G-protein coupled receptors (GPCRs) and ion channels, and host defense peptides.

- **MacroFinder:** The MacroFinder concept is based on non-peptidic, cell-permeable, and orally bioavailable macrocycles which can address complex and challenging intracellular targets.

Macrocycles are medium size cyclic molecules with a molecular weight (MW)-range of between 500 and 2,000 MW that complement the chemical space between small molecules (100-500 MW) and large molecules or so-called biopharmaceuticals (10,000-200,000 MW) and were designed to address complex and challenging extra- and intracellular biological targets with high unmet medical need. The macrocycle platform is applicable for many therapeutic areas and different target product profiles. The company's macrocycle library consists of over 50,000 single, untagged, individually purified peptidic and non-peptidic macrocycles readily amenable to all screening formats (binding, enzymatic, cellular pathway, phenotypical et cetera).

By screening the PEMfinder library and applying PEM technology, promising hits and leads were discovered, optimized, and further developed into clinical-stage compounds, including murepavadin with an intravenous (IV) and inhaled formulation, balixafortide, and lonodelestat (global rights sold to Santhera) as well as the OMPTA (Outer Membrane Protein Targeting Antibacterials) class of antibacterials targeting Gram-negative infections including WHO priority 1 Gram-negative infections with a high unmet medical need.

Macrocycle research partnerships were established with Novartis (2010), Boehringer Ingelheim (2012), Taisho (2015), Gilead (2016), and other companies to identify novel compounds against targets of the partners' interest.

The pipeline consists of several products targeting rare lung infections and cancer
Spexis pipeline consists of antibacterial therapeutics targeting chronic respiratory infections in rare diseases and CXCR4 inhibitors targeting cancer and non-cancer indications.

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH YEAR	PARTNERSHIP / FUNDING	PEAK SALES
COLIFIN	POLYMYXIN ANTIBACTERIAL	CYSTIC FIBROSIS P. AERUGINOSA INFECTIONS	PHASE III (US/ROW) LAUNCHED (EU)	2026 2010	GLOBAL RIGHTS (EXCL. EUROPE) ACQUIRED FROM PARI PHARMA; FUNDING BY CFF **	CHF 300+ MN
INHALED MUREPAVADIN	OMPTA CLASS* ANTIBACTERIAL	CYSTIC FIBROSIS P. AERUGINOSA INFECTIONS	PHASE IA	2028	FUNDING BY IMI ^ AND CFF **	CHF 200 MN
BALIXAFORTIDE	CXCR4 INHIBITOR	SINGLE AGENT/COMBO CANCER RARE DISEASE INDICATIONS	PRECLINICAL	TBD	FOSUN PHARMA (CHINA)	TBD
NEW CXCR4 LEAD CANDIDATE	CXCR4 INHIBITOR	HEMATOLOGICAL MALIGNANCIES	PRECLINICAL	TBD	TBD	TBD
LONODELESTAT (POL6014)	HUMAN NEUTROPHIL ELASTASE (HNE) INHIBITOR	CYSTIC FIBROSIS	PHASE I	>2025	GLOBAL RIGHTS ACQUIRED BY SANTHERA IN 2018	CHF 1 BN

* OMPTA = OUTER MEMBRANE PROTEIN TARGETING ANTIBIOTIC; ** CFF = CYSTIC FIBROSIS FOUNDATION; ^ IMI = INNOVATIVE MEDICINES INITIATIVE; ^^ CARB-X = COMBATING ANTIBIOTIC-RESISTANT BACTERIA BIOPHARMACEUTICAL ACCELERATOR
ESTIMATES AS OF 17 AUG 2022 SOURCE: SPEXIS, VALUATIONLAB ESTIMATES

Spexis's antibacterial therapeutics pipeline for rare diseases that typically require chronic treatment currently consists of the phase III-ready antibacterial therapeutic ColiFin, and phase I inhaled murepavadin, both in clinical development for treating chronic *P. aeruginosa* infections in cystic fibrosis. Additionally, Spexis is entitled to milestone payments and royalties on sales for lonodelestat from Santhera, which acquired the global rights in February 2018. Lonodelestat is an inhaled human neutrophil elastase (hNE) inhibitor that should start phase IIa POC trials in cystic fibrosis in 2022 (dependent on Santhera securing sufficient funding).

Its novel CXCR4 inhibitors include balixafortide and a new CXCR4 lead candidate focused on orphan, hematological malignancies, and potentially also non-oncology indications. Spexis is evaluating possible other cancer or non-oncology indications and combination therapies for balixafortide following the negative phase III "FORTRESS" trial results in advanced breast cancer in June 2021.

Spexis's key pipeline projects include:

1) RARE DISEASE ANTIBACTERIAL PIPELINE:

- **ColiFin for *P. aeruginosa* infection in cystic fibrosis**
  ColiFin is a polymixin antibacterial with the active ingredient colistin also named colistimethate sodium. Polymyxins are a group of basic cyclic polypeptides with activity against most Gram-negative bacteria and were first isolated from a Bacillus spp. in 1947. Five different chemical compounds (polymixins A, B, C, D, and E) are included in this group. Polymixin B and polymixin E (colistin) are the two polymixins that have been used therapeutically. Polymixin E, named colistin or colistimethate sodium, was isolated from Bacillus colistinus in 1950. On 12 February 2010, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) granted PARI Pharma EU approval for ColiFin (colistin) as a prescription-only medication to treat lung infections caused by the bacteria *Pseudomonas aeruginosa* in patients with cystic fibrosis. ColiFin is a powder that is inhaled using a nebulizer twice daily. More than 15,000 patients have been dosed so far in Europe with the drug becoming a front-line treatment for cystic fibrosis due to its low propensity for resistance development, reported efficacy and its favorable side effect profile.
  The global rights (excluding Europe) were licensed from PARI Pharma by Spexis to develop and commercialize ColiFin in the lucrative US market where a branded colistin product has not yet been approved for cystic fibrosis. In the US, colistin is widely

prescribed off-label under the instigation of a physician at their own risk with no formal pricing or reimbursement for cystic fibrosis. For US approval, the FDA requires only a single phase III trial in cystic fibrosis. In 2020, ColiFin was granted Qualified Infectious Disease Product (QIDP) and Orphan Disease designation providing 5 years and 7 years of market exclusivity for a total of 12 years from FDA approval. The company also received a phase III "Study May Proceed" letter from the FDA and "Fast Track" designation with the company eligible for Priority Review (6 months instead of 10 months) review. In 2021, the Cystic Fibrosis Foundation (CFF)'s Therapeutic Development Network (TDN) sanctioned the phase III trial design, and the CFF invested USD 2.4 mn in the pre-merger financing round of Spexis.

- **Inhaled murepavadin for *P. aeruginosa* infections in patients with cystic fibrosis**
  Murepavadin is Spexis' most progressed novel OMPTA (outer-membrane protein targeting antibiotic) class compound discovered entirely in-house from its proprietary macrocycle-based technology platform. Unfortunately, the intravenous formulation, murepavadin IV, which was in phase III development for severe hospital lung infections, had to be discontinued due to kidney injury in 2019. Fortunately, the company is also developing an inhaled formulation of murepavadin for the treatment of chronic *P. aeruginosa* infections in patients with cystic fibrosis and non-cystic fibrosis bronchiectasis (nCFBE).

  In the 7 clinical trials conducted to date, significant preclinical data demonstrated that inhaled murepavadin is highly potent at low doses with a high safety margin (at least 5- to 10-fold above the intravenous formulation), has rapid bacterial properties with best *in vitro* activity against *P. aeruginosa* including multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains, a low propensity to resistance and no cross-resistance with other therapeutics.

  In December 2020, a CTA (clinical trial application) was granted in the UK, and phase Ia development started in December 2021 (delayed to further optimize primary packaging to provide better stability for later stages of development). Safety results are expected in Q4 2022, and results in cystic fibrosis patients (Part C) are expected in mid-2023. A phase IIa proof-of-concept (POC) trial in cystic fibrosis patients is expected to start in late 2023 based on securing sufficient funding. The phase I program was partly funded up to 50% by the EU Innovative Medicines Initiative (IMI). The company was awarded a grant of up to USD 3.3 mn from the Cystic Fibrosis Foundation in November 2020. Spexis continues to seek further external funding.

- **Lonodelestat in cystic fibrosis – Spexis entitled to milestones and royalties by Santhera**
  Lonodelestat is a novel, highly potent, selective, and reversible inhibitor of human neutrophil elastase (hNE), one of the major lung-tissue degrading enzymes under pathological conditions and leading to respiratory decline and exacerbations in cystic fibrosis patients and many other lung diseases. Chronic inflammation is thought to be caused by neutrophil elastase from neutrophils present in the lung due to the buildup of thick mucus. High levels of hNE have been detected in cystic fibrosis sputa and these high levels of hNE correlate with disease severity and are measured by functional lung parameters such as FEV1 reduction and are therefore important surrogate markers of disease. Global rights were licensed to Santhera (ticker: SANN) in February 2018. Spexis is eligible for up to CHF 121 mn in development, regulatory, and sales milestones

and tiered royalties up to 10% on sales from Santhera. In early March 2021, Santhera reported positive multiple ascending dose (MAD) results. POC trials could start in 2022 (dependent on Santhera securing sufficient funding).

2) ONCOLOGY PIPELINE:

CXCR4 is a key target in cancer growth and metastasis with large promise

Spexis's immuno-oncology pipeline is focused on blocking the CXCR4 (C-X-C motif chemokine receptor 4) with its key compound balixafortide. CXCR4 is a chemokine receptor crucial in tumor progression and has been expressed in various types of cancers, including breast cancer and others. Overexpression of CXCR4 promotes tumor growth through increased signaling pathways, angiogenesis (new blood vessel formation), metastasis, and immune cell modulation. CXCR4-positive tumors often grow faster than CXCR4-negative tumors, while lymph node metastasis and distant organ metastasis frequently occur in CXCR4-positive tumor cases. CXCR4 is considered to be a factor of poor prognosis in cancer. Consequently, CXCR4 is a key target in cancer growth and metastasis. Sanofi's Mozobil (plerixafor) is the first approved CXCR4 antagonist. Mozobil was approved in the US (2008) and the EU (2009) to be used in combination with a granulocyte-colony-stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients living with multiple myeloma. Sales of Mozobil amounted to EUR 244 mn in 2020.

- **Balixafortide is a first-in-class CXCR4 antagonist for cancer and non-oncology indications**

  Balixafortide is a potent and selective CXCR4 antagonist targeted to improve treatment outcomes in cancer in combination with chemotherapy and cancer immunotherapy. Balixafortide is the most advanced CXCR4 antagonist in clinical development for solid tumors. Balixafortide has been investigated in eight clinical trials with a total of 501 subjects either as a single agent or in combination with other drugs. Six clinical trials have been completed to date. In May 2021, the company reported negative outcomes for the pivotal "FORTRESS" phase III trial of balixafortide in 432 patients with advanced breast cancer, with further development in advanced breast cancer terminated. Preclinical trials were also conducted to establish the potential of balixifortide in combination with other drugs (e.g., chemotherapy and immunotherapies) in metastatic breast cancer and in other cancer indications.

  Given the negative outcomes of the "FORTRESS" trial but also considering other clinical and preclinical data supporting a variety of additional cancer and non-oncology indications, Spexis is currently evaluating how to further develop balixafortide. A strategic decision is expected in H2 2022.

- **New CXCR4 lead compound for hematological malignancies**

  At the FY 2020 results, the company announced a new CXCR4 lead compound for hematological malignancies, targeting blood cancers such as lymphoma, leukemia, and myeloma. A patent application will be filed in H2 2022 and shortly thereafter the company is expected to disclose the compound and its potential lead indication(s). Blood cancers present a large untapped market opportunity and do not present a competitive threat for balixafortide, which is specifically developed for solid tumors.

In the following section, we will provide an in-depth analysis and forecasts for Spexis's key driver ColiFin in chronic *P. aeruginosa* infections in cystic fibrosis.

Forecasts & Sensitivity Analysis

ColiFin (cystic fibrosis)

Product Analysis

ColiFin in cystic fibrosis - Peak sales of CHF 300+ mn; rNPV of CHF 3.7/share
We forecast peak sales for North America (the US and Canada) to amount to CHF 344 mn for ColiFin in cystic fibrosis patients with P. aeruginosa infections. We assume Spexis to build up its own small specialist sales force to retain and maximize the long-term value in the lucrative US market with a launch expected in mid-2026 upon positive pivotal phase III "COPA" trial results expected in mid-2025 (NOTE: the US launch could occur roughly 9 months earlier upon positive "COPA" interim analysis trial results expected in late 2024/early 2025). In the US, ColiFin should enjoy at least 12 years of market exclusivity, consisting of 5 years of QIDP and 7 years of Orphan Drug market exclusivity. The US market provides a unique "switch" opportunity for ColiFin, with an estimated 36% of adult patients with moderate or advanced disease currently treated with off-label generic colistin. We forecast peak sales in this immediately capturable market of roughly 4,500 patients (4 treatment cycles per year at USD 6,600/cycle) to amount to approximately CHF 150 mn, with a rapid market penetration reaching 90% in just a few years. For other patients (not treated with off-label colistin), we forecast a gradual uptake and lower peak market penetration of ~30% in patients with advanced disease (8 treatment cycles per year) and ~15% in patients with moderate disease (4 treatment cycles per year), with peak sales for this patient group amounting to approximately CHF 200 mn. We account for M&S costs rising to around USD 15 mn and COGS of 20% (including royalties to PARI Pharma). Our rNPV amounts to CHF 584 mn, or CHF 3.7 per share, with a conservative 55% (phase III-ready) success rate and a WACC of 7% (for details, see page 21).

NOTE: Our success rate will increase to a historical 65% phase III success probability upon the start of the pivotal "COPA" phase III trial in H2 2023. This may be considered conservative, as ColiFin is already approved and on the market for cystic fibrosis in Europe, and generic colistin is widely prescribed off-label for cystic fibrosis in the US.

Attractive opportunity in the US with a relatively low risk

Spexis's most advanced pipeline project is ColiFin, a branded version of inhaled colistin for treating cystic fibrosis patients with chronic *P. aeruginosa* infection, the most common bacterial infection and reason for illness and death of patients. Spexis acquired the global rights (excluding Europe) of ColiFin from PARI Pharma, which distributes ColiFin in Europe since 2010. More than 15,000 patients have been dosed so far in Europe with the drug becoming a front-line treatment for cystic fibrosis due to its low propensity to resistance and favorable side effect profile. In the US, generic colistin has not been approved for treating *P. aeruginosa* infections in cystic fibrosis patients. Colistin is prescribed "off-label" at the instigation of a physician (with a potential liability risk) with no formal pricing and reimbursement for cystic fibrosis patients. Nevertheless, an estimated 36% of adult cystic fibrosis patients have been treated with colistin thanks to its favorable safety and tolerability profile with a low propensity to resistance compared to other inhaled antibacterial therapeutics such as Viatris's TOBI (tobramycin) Podhaler or Gilead's Cayston (aztreonam). This presents an attractive opportunity for Spexis to seek formal approval for branded

ColiFin. The FDA requires only a single phase III trial for US approval. Spexis plans to start its phase III "COPA" trial in H2 2023, with results due in mid-2025. Important to note is that ColiFin could be launched approximately one year earlier in the US market upon positive interim analysis trial results of "COPA" expected in late 2024/early 2025, after around 60% of patients have completed 28 days of treatment. Spexis could apply for US accelerated approval upon strong interim analysis "COPA" trial results.

Upon initiation of the phase III "COPA" trial, we will assume a conservative 65% phase III success probability; however, the development risk is likely lower as ColiFin is already approved in the EU with more than 15,000 patients dosed thus far.

Attractive "switch" opportunity leading to a rapid uptake of ColiFin in colistin patients
ColiFin could rapidly capture off-label colistin patients, providing physicians and patients with an FDA-approved alternative, and reducing the physician liability risk with formal pricing and reimbursement for cystic fibrosis patients. ColiFin should also capture a meaningful portion of patients treated with TOBI Podhaler or Cayston, as well as new patients, due to its superior profile. Assuming Priority Review (6 months instead of 10 months) based on granted Fast Track designation, the US launch is expected to occur in mid-2026. We forecast ColiFin's peak sales in North America to reach CHF 300+ mn in cystic fibrosis. To retain and maximize long-term value, Spexis plans to build its own small specialist sales force of approximately 20 FTEs to commercialize ColiFin in North America. Moreover, the sales force can be leveraged with a potential future approval of inhaled murepavadin in cystic fibrosis. The cash flow from ColiFin could also help fund the phase III development of inhaled murepavadin.

Lucrative US cystic fibrosis market
ColiFin targets a USD 3.9 bn US cystic fibrosis market or approximately 80% of the global market. According to Fortune Business Insights, the global cystic fibrosis market amounted to USD 5.1 bn in 2019 and is projected to grow by a staggering 24.4% CAGR to reach USD 31.9 bn by 2027. Growth will largely be boosted by the introduction of CFTR (cystic fibrosis transmembrane conductance regulator) modulators, a new class of disease-modifying compounds, that improve the body's function at the cellular level. Vertex is expected to dominate this market with its unique offering of multiple approved CFTR modulators. Nevertheless, inhaled antimicrobial treatments like ColiFin should still be able to enjoy strong growth. CFTR modulators are expected to further prolong life expectancy in cystic fibrosis patients which increases the susceptibility to chronic lung infections despite the use of these novel agents.

ColiFin appears to have a superior profile with the potential for once-daily dosing
ColiFin appears to have a superior safety and tolerability profile compared to in-market branded inhaled antibacterial therapeutics such as Viatris's TOBI (tobramycin) and Gilead's Cayston (aztreonam) with a lower propensity to resistance and the potential to once-daily dosing.

COMPARISON OF INHALED ANTIBIOTICS TO TREAT P. AERUGINOS INFECTION IN PATIENTS WITH CYSTIC FIBROSIS		
	TOBI (TOBRAMYCIN) **/ CAYSTON** (AZTREONAM)	**COLIFIN** (COLISTIN)
MECHANISM OF ACTION	LENDS TO RESISTANCE DEVELOPMENT	DIFFICULT FOR P. AERUGINOSA TO MUTATE AROUND
RESISTANCE RATES	INCREASING, UP TO 40% IN SOME REGIONS	RARELY EXCEEDING ~5%
SAFETY	TOBI HAS SIGNIFICANT OTOTOXICITY CONCERNS	LATEST EU-POST MARKETING SAFETY ANALYSES SHOW NO REPORTED DRUG-RELATED OTO/NEURO/NEPHROTOXICITIES
EFFICACY	DECREASED EFFICACY OVER TIME	FRONT-LINE AGENT IN EUROPE OVER TOBI AND CAYSTON
DOSING	2X TO 4X DAILY DOSING WITH CONTINUOUS ALTERNATING THERAPY PER TREATMENT CYCLE	CONTINUOUS 2X OR EVEN 1X (IF "COPILOT" IS POSITIVE) DAILY DOSING

SOURCE: SPEXIS, VALUATIONLAB

As can be seen in the table above, ColiFin has a significantly lower resistance rate than the TOBI/Cayston inhaled antibacterial therapeutics, rarely exceeding 5% compared to an increasing, up to 40% resistance rate in some regions, due to the difference of mechanism of action. In ColiFin it is difficult for *P. aeruginosa*, responsible for two-thirds of chronic lung infections in patients, to mutate around. TOBI has significant ototoxicity concerns including hearing loss or tinnitus, the perception of sound when no external sound is present often described as a ringing sound. In Europe, ColiFin is used as a front-line agent over TOBI/Cayston as both experience decreased efficacy over time. As a result, TOBI and Cayston often require continuous alternating therapy (CAT), for instance, one treatment cycle (28 days) on TOBI and on the next treatment cycle switching to Cayston to avoid loss in efficacy and the development of bacterial resistance. Moreover, TOBI requires twice-daily dosing, while Cayston can require dosing up to 4 times a day with a cumbersome nebulizer. A nebulizer is a small machine that turns a liquid drug into a mist to enhance the uptake in the lungs. The patient is required to take slow, deep breaths for 10 to 15 minutes. Spexis will evaluate the tolerability and safety of once-daily compared to twice-daily dosing of ColiFin by a nebulizer in the “COPILOT” dosing trial. If positive, this would be another unique selling point for ColiFin.

ColiFin validated by significant progress in the US clinical development program

After in-licensing the global rights (excluding Europe) of ColiFin from PARI Pharma, the company has made significant progress in the US clinical development program. Spexis received positive FDA feedback on its clinical registration strategy. The FDA communicated that only a single pivotal phase III trial was needed to receive US approval for treating *P. aeruginosa* infection in cystic fibrosis patients. In February 2020, the FDA granted Qualified Infectious Disease Product (QIDP) designation for ColiFin, providing 5 years of market exclusivity in the US from FDA approval, a special incentive for companies that develop novel anti-infectives for the US market. In March 2020, ColiFin received Orphan Drug designation from the FDA, providing 7 years of market exclusivity from US approval and extending ColiFin’s US market exclusivity to a total of at least 12 years. Orphan Drug designation is an incentive for companies that develop new treatments for rare diseases that affect fewer than 200,000 patients in the US. In April 2020, the Investigation New Drug (IND) application was submitted to the FDA with the company receiving a phase III “Study May Proceed” letter from the FDA in May 2020. In November 2020, ColiFin received Fast Track designation allowing for an expedited review of 6 months instead of 10 months. Fast Track designation is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need.

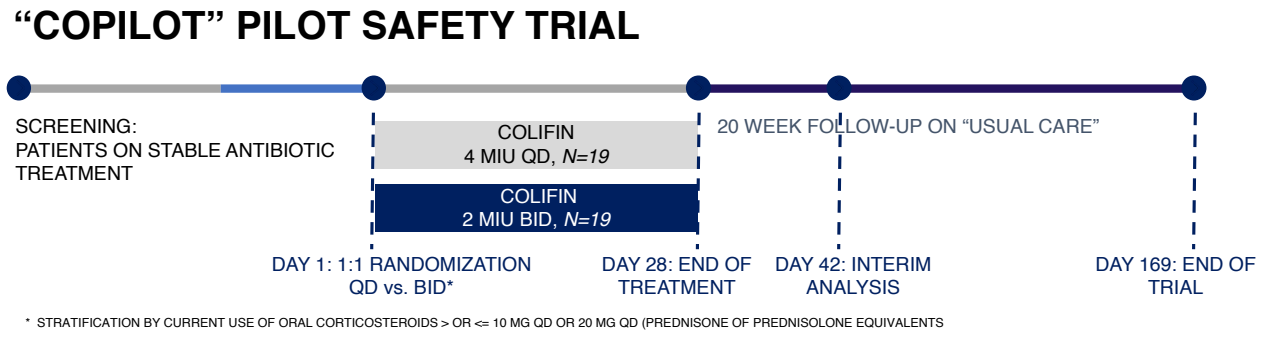
We believe the swift and positive interaction with the FDA underlines the importance of

providing US cystic fibrosis patients with an FDA-approved alternative to off-label colistin, with a potentially superior dosing profile to current in-market inhaled antibacterial therapeutics which are used chronically. Further validation of the potential value of ColiFin in the US is the Cystic Fibrosis Foundation (CFF)'s Therapeutic Development Network sanctioning of the pivotal phase III trial design and the USD 2.4 mn investment by the CFF in the pre-merger financing round in December 2021, in our view.

The clinical development program consists of the "COPILOT" dosing trial, and the phase III pivotal "COPA" trial – The program starts H1 2023; results mid-2025; NDA submission H2 2025

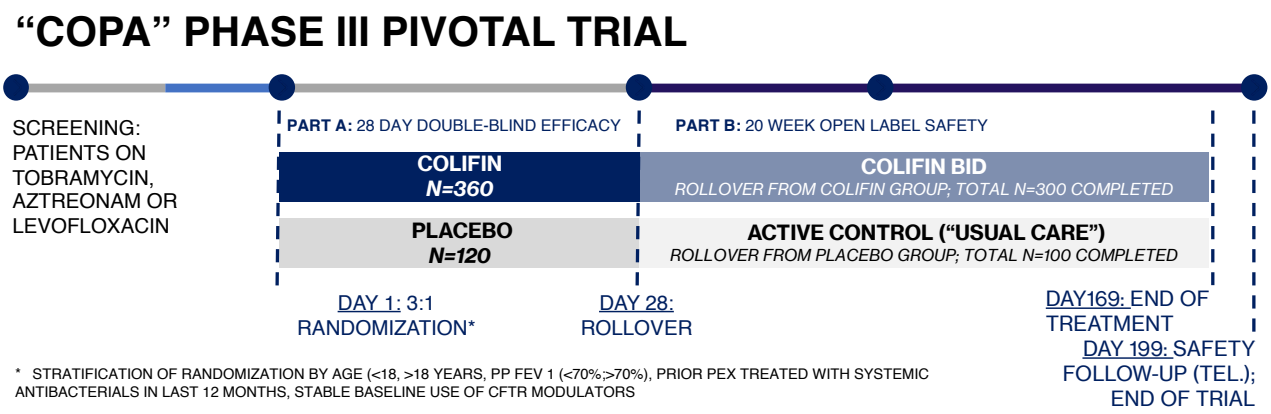
The US clinical development program for ColiFin in cystic fibrosis consists of two trials:

1) **"COPILOT" phase III dosing pilot trial:** A targeted 38 cystic fibrosis patients will be equally randomized over two treatment arms consisting of 19 patients treated on either once-daily or twice-daily ColiFin for 28 days (one treatment cycle), followed by a 20-week "usual care" follow-up. Spexis plans to start the trial in H1 2023 with topline results in H2 2023, to assess whether ColiFin can be given once daily, potentially providing an additional USP compared to competitor drugs, which have to be given twice or three times daily with a nebulizer.



2) **"COPA" phase III pivotal trial:** A targeted 480 cystic fibrosis patients on tobramycin, aztreonam, or levofloxacin will be randomized 3:1 to two treatment arms consisting of 1) 360 patients treated with ColiFin once-daily (if "COPILOT" is positive, otherwise twice-daily), and 2) 120 patients treated with placebo with the same dosing regimen as ColiFin. The trial consists of two efficacy parts: 1) Part A: evaluates double-blind efficacy at Day 28 (one treatment cycle), and 2) Part B: 20-week open-label safety rollover to open-label ColiFin or open-label usual care (for patients randomized to placebo) expected at least 300 patients dosed on for 6 months with ColiFin, and 100 patients 1 month on placebo followed by 5 months of "usual care" at Day 169. The primary endpoint is the mean absolute difference in percent predicted forced expiratory volume in 1 second (ppFEV1) of ≥3% in change from baseline to Day 28. Key secondary endpoints throughout 6 months include the difference in CFQ-R respiratory symptom score, evaluate exacerbation severity/duration; consistency of treatment response; microbiology in sputum: *P. aeruginosa* density; and resistance development (MIC).

   An interim efficacy analysis is planned after 60% of patients have completed treatment on Day 28 (Part A) in late 2024/early 2025. The trial is expected to start in H2 2023, concurrent with the "COPILOT" follow-up.



SOURCE: SPEXIS, VALUATIONLAB

Upon positive "COPA" trial results, Spexis plans to file the New Drug Application (NDA) for ColiFin in H2 2025. We assume Priority Review (6 months instead of 10 months) based on the Fast Track designation granted by the FDA in November 2020. Consequently, ColiFin could be approved and launched in the US by H1 2026.
Important to note is that positive "COPA" interim analysis results expected to report in late 2024/early 2025 could lead to US accelerated approval and an earlier US launch by approximately one year.

North America's detailed bottom-up forecasts point to CHF 300+ mn peak sales in CF
It is estimated that in the US there are roughly 30,000 cystic fibrosis patients in the US of which approximately 20,000 are adults. This amounts to a prevalence of approximately 50 adult cystic fibrosis patients per 1 mn people in the US. We have applied the same prevalence rate for Canada to come to our patient numbers for North America. An estimated ~15% of cystic fibrosis patients have advanced disease, ~45% moderate disease, with P. aeruginosa causing roughly two-thirds of chronic lung infections requiring chronic treatment with an inhaled antibacterial.

With an estimated 36% of adult patients with moderate or advanced disease treated with off-label colistin, the US market provides a unique "switch" opportunity for ColiFin, providing physicians and patients with an FDA-approved alternative with formal pricing and reimbursement for cystic fibrosis. We forecast peak sales in this immediately capturable market of roughly 4,500 patients to amount to approximately CHF 150 mn, with a rapid market penetration reaching 90% in just a few years, conservatively assuming 4 treatment cycles per patient in a year, with a treatment cost of USD 6,600 per cycle (28 days treatment).

For cystic fibrosis patients (not treated with colistin) and new patients, we forecast a more gradual uptake with a lower peak market penetration of ~30% in patients with advanced disease with 8 treatment cycles per year (at USD 6,600 per treatment cycle). For patients with moderate disease, we forecast a peak market penetration of ~15% in patients and 4 treatment cycles per year. Peak sales for new patients are forecast to amount to approximately CHF 200 mn. We calculate an rNPV of CHF 584 mn or CHF 3.7/share for ColiFin in cystic fibrosis, with a conservative 55% (phase III-ready) success probability and a WACC of 7%.

NOTE: Our success probability will increase to a historical 65% phase III rate upon the start of the phase III "COPA" trial in H2 2023, which can be considered conservative, as ColiFin is already approved in the EU and generic colistin is widely prescribed off-label in the US.

Forecasts & Sensitivity Analysis

COLIFIN - FINANCIAL FORECASTS FOR CYSTIC FIBROSIS

INDICATION	TREATMENT OF CHRONIC PSEUDOMONAS AERUGINOSA LUNG INFECTION IN PATIENTS WITH CYSTIC FIBROSIS
DOSAGE	INHALATION 1-2 MIU (MEGA INTERNATIONAL UNITS) THREE TIMES DAILY FOR UP TO 8 MONTHS IN CONJUNCTION WITH OTHER ANTIBIOTICS
PRICE	ANNUAL TREATMENT COST PER PATIENT: US: USD 6,600/CYCLE - COLISTIN SWITCH PATIENTS 4 CYCLES, ADVANCED PATIENTS 8 CYCLES, MODERATE PATIENTS 4 CYCLES
STANDARD OF CARE	PARI PHARMA'S COLIFIN (INHALED COLISTIN) - EU ONLY; US: GENERIC COLISTIN, VIATRIS' TOBI PODHALER (INHALED TOBRAMYCIN); GILEAD'S CAYSTON (INHALED AZTREONAM)
UNIQUE SELLING POINT	STRONG EFFICACY, MINIMAL SAE'S; FRONT LINE RX IN EU

7Ps ANALYSIS

PATENT	ORPHAN DRUG DESIGNATION (ODD) AND QUALIFIED INFECTIOUS DISEASE PRODUCT (QIDP) GRANTED PROVIDE 12 YEARS US MARKET EXCLUSIVITY UPON APPROVAL
PHASE	APPROVED IN EU SINCE 2010; US: PHASE III DEVELOPMENT TO START H1 2023, NDA SUBMISSION H2 2025, APPROVAL H1 2026 (ASSUMES FAST TRACK REVIEW)
PATHWAY	SINGLE US PHASE III TRIAL REQUIRED FOR US APPROVAL; FAST TRACK DESIGNATION RECEIVED THAT GUARANTEES EXPEDITED (6-MONTHS) REVIEW
PATIENT	FORMAL PRICING AND REIMBURSEMENT ALLOWS FOR HIGHER UPTAKE OF THIS EFFECTIVE AND SAFE TREATMENT FOR P. AERUGINOSA INFECTIONS IN CYSTIC FIBROSIS
PHYSICIAN	ADDITIONAL FDA-APPROVED INHALED ANTIBIOTIC TO TREAT INFECTION AND INFLAMMATION CAUSED BY P. AERUGINOSA INFECTION IN PATIENTS WITH CYSTIC FIBROSIS
PAYER	LESS CONTINUOUS ALTERNATING THERAPY AND LOWER PRICING THAN CURRENT IN-MARKET INHALED PRODUCTS SHOULD LEAD TO LOWER OVERALL TREATMENT COSTS
PARTNER	WW RIGHTS (EXCL. EUROPE) ACQUIRED FROM PARI PHARMA; SPEXIS PLANS TO BUILD UP ITS OWN US SPECIALIST SALES FORCE TO RETAIN AND MAXIMIZE LONG-TERM VALUE

REVENUE MODEL

NORTH AMERICA (UNITED STATES & CANADA) - SPEXIS SALES FORCE	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
NUMBER OF ADULT CF PATIENTS	19,870	20,466	21,080	21,712	22,364	23,034	23,725	24,437	25,170	25,925	26,703
GROWTH (%)	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
MODERATE/ADVANCED CF PATIENTS (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
MODERATE/ADVANCED CF PATIENTS	11,922	12,279	12,648	13,027	13,418	13,821	14,235	14,662	15,102	15,555	16,022
PATIENTS TREATED WITH OFF-LABEL COLISTIN (%)	36%	36%	36%	36%	36%	36%	36%	36%	36%	36%	36%
PATIENTS TREATED WITH OFF-LABEL COLISTIN	4,292	4,421	4,553	4,690	4,831	4,975	5,125	5,278	5,437	5,600	5,768
PENETRATION (%)	0%	0%	0%	0%	0%	5%	60%	90%	90%	90%	90%
OFF-LABEL COLISTIN PATIENTS TREATED WITH COLIFIN	**0**	**0**	**0**	**0**	**0**	**249**	**3,075**	**4,751**	**4,893**	**5,040**	**5,191**
NUMBER OF TREATMENT CYCLES PER YEAR	4	4	4	4	4	4	4	4	4	4	4
COST OF THERAPY PER CYCLE (CHF)	6,009	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174
ANNUAL COST OF THERAPY PER PATIENT (CHF)	24,035	24,694	24,694	24,694	24,694	24,694	24,694	24,694	24,694	24,694	24,694
SALES CF "SWITCH" PATIENTS (FROM OFF-LABEL COLISTIN TO COLIFIN)	**0**	**0**	**0**	**0**	**0**	**6**	**76**	**117**	**121**	**124**	**128**
PATIENTS WITH ADVANCED DISEASE (%)	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
PATIENTS WITH ADVANCED DISEASE	2,980	3,070	3,162	3,257	3,355	3,455	3,559	3,666	3,776	3,889	4,005
PATIENTS WITH P. AERUGINOSA INFECTION (%)	66%	66%	66%	66%	66%	66%	66%	66%	66%	66%	66%
ADVANCED PATIENTS WITH P. AERUGINOSA INFECTION	1,967	2,026	2,087	2,150	2,214	2,280	2,349	2,419	2,492	2,567	2,644
ADVANCED PATIENTS NOT ON OFF-LABEL COLISTIN (%)	64%	64%	64%	64%	64%	64%	64%	64%	64%	64%	64%
ADVANCED PATIENTS NOT ON OFF-LABEL COLISTIN	1,259	1,297	1,336	1,376	1,417	1,459	1,503	1,548	1,595	1,643	1,692
PENETRATION (%)	0%	0%	0%	0%	0%	4%	10%	14%	18%	22%	26%
ADULT CF PATIENTS ADVANCED DISEASE TREATED	**0**	**0**	**0**	**0**	**0**	**58**	**150**	**217**	**287**	**361**	**440**
NUMBER OF TREATMENT CYCLES PER YEAR	8	8	8	8	8	8	8	8	8	8	8
COST OF THERAPY PER CYCLE (CHF)	6,009	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174
ANNUAL COST OF THERAPY PER PATIENT (CHF)	48,070	49,388	49,388	49,388	49,388	49,388	49,388	49,388	49,388	49,388	49,388
COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES ADULT CF PATIENTS ADVANCED DISEASE (CHF MN)	**0**	**0**	**0**	**0**	**0**	**3**	**7**	**10**	**13**	**16**	**20**
PATIENTS WITH MODERATE DISEASE (%)	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%
PATIENTS WITH MODERATE DISEASE (%)	8,941	9,210	9,486	9,770	10,064	10,366	10,676	10,997	11,327	11,666	12,016
PATIENTS WITH P. AERUGINOSA INFECTION (%)	66%	66%	66%	66%	66%	66%	66%	66%	66%	66%	66%
MODERATE PATIENTS WITH P. AERUGINOSA INFECTION	5,901	6,078	6,261	6,449	6,642	6,841	7,046	7,258	7,476	7,700	7,931
ADVANCED PATIENTS NOT ON OFF-LABEL COLISTIN (%)	64%	64%	64%	64%	64%	64%	64%	64%	64%	64%	64%
ADVANCED PATIENTS NOT ON OFF-LABEL COLISTIN	3,777	3,890	4,007	4,127	4,251	4,378	4,510	4,645	4,784	4,928	5,076
PENETRATION (%)	0%	0%	0%	0%	0%	2%	5%	7%	9%	11%	13%
ADULT CF PATIENTS MODERATE DISEASE TREATED	**0**	**0**	**0**	**0**	**0**	**88**	**225**	**325**	**431**	**542**	**660**
NUMBER OF TREATMENT CYCLES PER YEAR	4	4	4	4	4	4	4	4	4	4	4
COST OF THERAPY PER CYCLE (CHF)	6,009	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174	6,174
ANNUAL COST OF THERAPY PER PATIENT (CHF)	24,035	24,694	24,694	24,694	24,694	24,694	24,694	24,694	24,694	24,694	24,694
COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES ADULT CF PATIENTS MODERATE DISEASE (CHF MN)	**0**	**0**	**0**	**0**	**0**	**9**	**77**	**118**	**125**	**132**	**140**
SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**18**	**159**	**245**	**258**	**273**	**288**
CHANGE (%)							810%	54%	6%	6%	5%
COGS (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
COGS (CHF MN)	0	0	0	0	0	-4	-32	-49	-52	-55	-58
M&S COSTS (CHF MN)	0	0	0	0	0	-7	-9	-11	-13	-13	-14
R&D COSTS (CHF MN)	0	0	-13	-23	-16	-1	0	0	0	0	0
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**-13**	**-23**	**-16**	**6**	**118**	**184**	**194**	**205**	**216**
TAX RATE (%)	0%	0%	0%	0%	0%	0%	0%	0%	5%	10%	15%
TAXES (CHF MN)	0	0	0	0	0	0	0	0	-10	-20	-32
PROFIT (CHF MN)	**0**	**0**	**-13**	**-23**	**-16**	**6**	**118**	**184**	**184**	**184**	**184**

	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**18**	**159**	**245**	**258**	**273**	**288**
CHANGE (%)							810%	54%	6%	6%	5%
GLOBAL PROFIT (CHF MN)	**0**	**0**	**-13**	**-23**	**-16**	**6**	**118**	**184**	**184**	**184**	**184**
CHANGE (%)			2600%	85%	-32%	-135%	2012%	56%	0%	0%	0%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**1,062**	
NUMBER OF SHARES (MN)	158.1	
NPV PER SHARE (CHF)	**7**	
SUCCESS PROBABILITY	55%	= PHASE III READY
RISK ADJUSTED NPV PER SHARE (CHF)	**3.7**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	7.8	7.4	7.1	6.7	6.4	6.1	5.8
	90%	7.0	6.7	6.4	6.0	5.8	5.5	5.2
	80%	6.2	5.9	5.6	5.4	5.1	4.9	4.6
	70%	5.5	5.2	4.9	4.7	4.5	4.3	4.1
SUCCESS PROBABILITY	60%	4.7	4.5	4.2	4.0	3.8	3.7	3.5
	55%	4.3	4.1	3.9	**3.7**	3.5	3.3	3.2
	50%	3.9	3.7	3.5	3.4	3.2	3.0	2.9

ESTIMATES AS OF 17 AUG 2022

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

ColiFin is likely to be the first FDA-approved and branded version of inhaled colistin for treating chronic P. aeruginosa infection in cystic fibrosis patients, with superior safety and tolerability profile and a lower propensity for resistance development than the current in-market, inhaled antibacterial therapeutics, the potential of once-daily dosing compared to at least twice daily dosing and no continuous alternating therapy (CAT) to reduce the risk of resistance and loss of efficacy.

7P's Analysis

Patent: ColiFin is not protected by patents, which have already expired approximately 5 years ago. ColiFin should enjoy at least 12 years of market exclusivity in the US, consisting of 5 years of Qualified Infectious Disease Product (QIDP) and 7 years of Orphan Drug market exclusivity from FDA approval. We expect the US launch in mid-2026. NOTE: A positive interim analysis of the pivotal "COPA" trial, expected to report in late 2024/early 2025, could potentially lead to an earlier US launch by roughly one year.

Pathway: ColiFin received the FDA Fast Track designation in November 2020 and is therefore eligible for expedited review, speeding up the US review time to only 6 months instead of 10 months.

Patient: The superior safety and tolerability profile of inhaled generic colistin with a low propensity of resistance is already a key driver for ~36% of adult patients to prefer this inhaled antibacterial therapeutic over TOBI and Cayston; however, there is no formal pricing and reimbursement for colistin in cystic fibrosis. FDA-approved ColiFin would receive formal pricing and reimbursement leading to easier patient access and lower patient (co)payments.

Physician: provides physicians with an FDA-approved version of inhaled colistin, which is currently prescribed off-label at the instigation of a physician and at their own risk. ColiFin would considerably reduce the potential liability risk for a physician currently prescribing unapproved inhaled colistin for cystic fibrosis.

Payer: Although branded ColiFin is expected to be priced higher than generic off-label inhaled colistin, physicians and patients not opting for off-label colistin due to lack of formal reimbursement, will frequently revert to TOBI and/or Cayston. ColiFin provides a better alternative to these branded treatments with a superior safety and tolerability profile with a low propensity of resistance and less need for continuous alternating therapy, and that at an expected lower pricing for ColiFin.

Partner: Spexis plans to build up its own small specialist sales force of approximately 20 FTEs in the US to maximize long-term value in the lucrative US market. The company can leverage its US sales force with the potential future approval of its inhaled murepavadin, a truly novel inhaled antibacterial for treating P. aeruginosa infection in cystic fibrosis patients. Moreover, the cash flow from ColiFin could be used to help finance the two phase III trials required for approval of inhaled murepavadin in cystic fibrosis in the US and the EU.

Cystic Fibrosis Market

The cystic fibrosis market amounted to USD 5.1 bn in 2019 and is projected to reach USD 31.9 bn by 2027 with a 24.4% CAGR during the forecast period, according to Fortune Business Insights. Growth should come from 1) an increasing number of patients globally with around 1,000 new cases diagnosed every year, 2) treatments that improve quality of life and prolong life expectancy, and 3) new treatments such as the CFTR (cystic fibrosis transmembrane conductance regulator) modulators are expected to account for the highest revenues. North America is the largest market due to the higher treatment costs and the number of treated patients with sales amounting to USD 3.9 bn (~76% of global sales) and is anticipated to dominate the market globally. Europe is considered to hold the second leading position owing to an increase in the prevalence of the disease and the rise in the adoption of novel drugs with better outcomes such as CFTR modulators. Vertex is expected to dominate the market with its unique offering of multiple approved CFTR modulators.

CYSTIC FIBROSIS - KEY FACTS	
MARKET SIZE	APPROXIMATELY USD 5 BN IN 2019 INCREASING WITH A 24% CAGR TO AROUND USD 32 BN IN 2027
PREVALENCE	>70,000 PATIENTS WORLDWIDE; >30,000 PATIENTS IN THE US
INCIDENCE	1 IN 25 TO 30 PEOPLE OF EUROPEAN DESCENT IS CARRIER OF THE CF MUTATION (HIGHEST IS IRELAND WITH 1 IN 1,352); 1 IN 46 IN HISPANICS; 1 IN 66 IN AFRICANS; 1 IN 90 IN ASIANS
UNDERLYING CAUSE	A PROGRESSIVE, GENETIC DISEASE THAT CAUSES CHRONIC LUNG INFECTIONS AND LIMITS THE ABILITY TO BREATHE OVER TIME; MUTATIONS IN THE CYSTIC FIBROSIS CONDUCTANCE REGULATOR (CFTR) GENE CAUSE THE CFTR PROTEIN TO BECOME DYSFUNTIONAL, UNABLE TO MOVE CHLORIDE (A COMPONENT OF SALT) TO THE CELL SURFACE. WITHOUT THE CHLORIDE TO ATTRACT WATER TO THE SURFACE, THE MUCUS IN VARIOUS ORGANS BECOMES THICK AND STICKY
SYMPTOMS	- CHRONIC LUNG INFECTIONS OR PNEUMONIA - WHEEZING - COUGHING WITH THICK MUCUS - BULKY, GREASY BOWEL MOVEMENTS - CONSTIPATION OR DIARRHEA - TROUBLE GAINING WEIGHT OR POOR HEIGHT GROWTH - SALTY SKIN AND VERY SALTY SWEAT LUNG PROBLEMS ARE RESPONSIBLE FOR DEATH IN ~80% OF PEOPLE WITH CYSTIC FIBROSIS
DRUG THERAPY (KEY BRANDS)	CURRENTLY THERE IS NO CURE FOR CYSTIC FIBROSIS, HOWEVER SEVERAL TREATMENT METHODS ARE USED IMPROVING LIFE EXPECTANCY FROM PREVIOUSLY LESS THAN ONE YEAR TO BETWEEN 42 AND 50 YEARS; TREATMENTS INCLUDE: ANTIBIOTICS (ONE OR MORE AT ALL TIMES TO PROPHYLACTICALLY SUPPRESS INFECTION), INCLUDING INHALED ANTIBIOTICS: - TOBRAMYCIN (TOBI PODHALER) - COLISTIMETHATE (COLISTIN, COLIFIN, XYLISTIN, COLOBREATHE) - AZTREONAM (CAYSTON) AEROLIZED MEDICATIONS THAT LOOSEN SECRETION: - DORNASE ALFA (PULMOZYME) - HYPERTONIC SALINE CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATORS (CFTR) MODULATORS: - IVACAFTOR (KALYDECO) - IVACAFTOR/TEZACAFTOR COMBO (SYMDECO/SYMKEVI) - LUMACAFTOR/IVACAFTOR COMBO (ORKAMBI) - IVACAFTOR/TEZACAFTOR/ELEXACAFTOR COMBO (TRIKAFTA/KAFTRIO)
MAJOR PLAYERS (KEY BRANDS)	- VERTEX (KALYDECO, SYMDECO/SYMKEVI, ORKAMBI, TRIKAFTA/KAFTRIO) - VIATRIS (TOBI PODHALER) - GILEAD (CAYSTON) - PARI PHARMA (COLIFIN - EUROPE ONLY) - SPEXIS (COLIFIN - WW EXCL. EUROPE) - ROCHE/GENENTECH (PULMOZYME)

SOURCE: VALUATIONLAB, NIH, CYSTIC FIBROSIS FOUNDATION, MAYO CLINIC, FORTUNE BUSINESS INSIGHTS, COMPANY REPORTS

Cystic fibrosis (CF) is a rare inherited disorder that causes severe damage to the lungs, digestive system and other organs in the body. The name cystic fibrosis refers to the characteristic fibrosis and cysts that form within the pancreas. It is caused the the presence of mutation in both copies of the gene for the cystic fibrosis transmembrane conductance regulator (CFTR) protein, and is inherited in an autosomal recessive manner. Those with a single working copy are carriers and otherwise mostly healthy. The disease only occures when two of these carriers have children. Different patients have different degrees of symptoms. The CFTR protein is a chloride ion channel important in creating sweat, digestive fluids, and mucus. These secreted fluids are normally thin and slippery and act as lubricants.

When the CFTR is not functional, these secretions become thick and sticky and plug up tubes, ducts, and passageways, especially in the lungs and pancreas.

Cystic fibrosis is most common among people of Northern European ancestry and affects about one out of every 3,000 newborns, with up to one in 25 people a carrier (the highest in Ireland with 1 in 1,352 people). Cystic fibrosis is present in other races, though not as frequently as in white individuals. About 1 in 46 Hispanics, 1 in 65 Africans, and 1 in 90 Asians carry a mutation of the cystic fibrosis gene. Cystic fibrosis typically manifests early in life. Newborns and infants with cystic fibrosis tend to have frequent, large, greasy stools (a result of malabsorption) and are underweight for their age. Newborn screening, improved care, and clinical awareness has contributed to decreased pediatric mortality and a stable and continuously growing cystic fibrosis adult population exceeding the pediatric population. Cystic fibrosis has become a chronic illness that affects the digestive and respiratory tracts resulting in generalized malnutrition and chronic lung infections. The primary cause of morbidity and death is lung failure in ~80% of patients. The average life expectancy is between 42 and 50 years in the developed world.

Major complications of cystic fibrosis include, among others:

- **Respiratory complications** such as damaged airways (bronchiectasis), chronic lung infections, growths in the nose, coughing up blood, collapsed lung (pneumothorax), acute exacerbations, and over time, respiratory failure, the most common cause of death.
- **Digestive system complications** such as nutritional deficiencies (thick mucus blocks enzymes from the pancreas to the intestines leading to poor absorption of proteins and fats), diabetes, liver disease, intestinal obstruction or distal intestinal obstruction syndrome (DIOS), a partial or complete obstruction where the small intestine meets the large intestine (colon), which requires urgent treatment.

Management of cystic fibrosis is still largely targeted at symptom treatment

While no cures for cystic fibrosis are known, several treatments are used, including:

- **Antibacterials** given by oral/intravenous or subcutaneous formulations are mainly used to treat acute or acutely worsening chronic (lung) infections. Inhaled antibacterial therapeutics such as Viatris' TOBI (tobramycin) Podhaler, Gilead's Cayston (aztreonam), and PARI Pharma's ColiFin (colistimethate) are mainly used as long-term treatments to better control chronic lung infections with P. aeruginosa or other bacteriae and avoid acute worsenings that often result in a further irreversible decline in lung function.
- **Mucolytics** such as aerosolized medications that help loosen secretions include Roche/Genentech's Pulmozyme (dornase alfa) or hypertonic saline.
- **Bronchodilators** help keep the airways open by relaxing the muscles around the bronchial tubes.
- **Pancreatic enzyme replacement therapy** includes oral pancreatic enzymes to help the digestive tract absorb nutrients
- **Cystic fibrosis transmembrane conductance regulator (CFTR) modulators** restore some effectiveness of the CFTR protein so that it can work as an ion channel on the cell's surface and is dominated by Vertex with Kalydeco (ivacaftor), Symdeko (ivacaftor/tezacaftor combo), Orkambi (lumacaftor/ivacaftor combo), and Trikafta (elexacaftor/tezacaftor/ivacaftor combo)
- **Gene therapy** is aimed at trying to place a normal copy of the CFTR gene into affected cells. Multiple approaches have been tested for gene transfer such as liposomes and viral vectors, however, these methods were so far found to be relatively inefficient treatment options.

Income Statement

SPEXIS									SHARE PRICE (CHF)	0.82	
IFRS											
INCOME STATEMENT (CHF MN)	**2021**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
PRODUCT SALES (INCL. PARTNER SALES)	**0**	**0**	**0**	**0**	**0**	**18**	**159**	**245**	**258**	**273**	**288**
CHANGE (%)							810%	54%	6%	6%	5%
PRODUCT SALES (SPEXIS SALES FORCE)	**0**	**0**	**0**	**0**	**0**	**18**	**159**	**245**	**258**	**273**	**288**
CHANGE (%)							810%	54%	6%	6%	5%
ROYALTIES	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**2.0**	**6.2**	**9.9**	**14.2**	**20.3**	**25.0**
CHANGE (%)							215%	60%	44%	43%	23%
UPFRONT AND MILESTONE PAYMENTS	**0.0**	**1.0**	**4.0**	**0.0**	**10.0**	**5.0**	**30.0**	**5.0**	**0.0**	**0.0**	**20.0**
CHANGE (%)			300%	-100%		-50%	500%	-83%	-100%		
OTHER REVENUES	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
CHANGE (%)											
REVENUES (EXCL. PARTNER SALES)	**0.0**	**1.0**	**4.0**	**0.0**	**10.0**	**24.5**	**195.5**	**259.4**	**272.5**	**292.9**	**332.6**
CHANGE (%)			300%	-100%		145%	699%	33%	5%	7%	14%
COGS	**0**	**0**	**0**	**0**	**0**	**-4**	**-32**	**-50**	**-57**	**-67**	**-72**
CHANGE (%)							810%	58%	14%	16%	9%
GROSS PROFIT	**0.0**	**1.0**	**4.0**	**0.0**	**10.0**	**21.0**	**163.6**	**209.0**	**215.0**	**226.4**	**260.2**
CHANGE (%)			300%	-100%		110%	680%	28%	3%	5%	15%
MARGIN (%)		100%	100%		100%	86%	84%	81%	79%	77%	78%
RESEARCH & DEVELOPMENT	**-0.9**	**-9.4**	**-31.4**	**-35.9**	**-16.9**	**-5.4**	**-24.5**	**-24.5**	**-24.5**	**-24.5**	**-24.5**
CHANGE (%)		970%	235%	15%	-53%	-68%	351%	0%	0%	0%	0%
MARKETING & SALES	**-0.1**	**-0.1**	**-0.1**	**-0.1**	**-0.1**	**-7.6**	**-10.4**	**-15.0**	**-16.0**	**-16.2**	**-16.5**
CHANGE (%)		2%	2%	2%	2%	9856%	37%	45%	6%	2%	2%
GENERAL & ADMINISTRATIVE	**-3.3**	**-8.0**	**-8.0**	**-8.0**	**-8.1**	**-8.2**	**-8.2**	**-8.3**	**-8.4**	**-8.5**	**-8.6**
CHANGE (%)	360%	142%	0%	0%	1%	1%	1%	1%	1%	1%	1%
OTHER INCOME (E.G. GRANTS)	**0.0**	**3.0**	**3.0**	**3.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
OPERATING COSTS	**-4.2**	**-14.4**	**-36.4**	**-41.0**	**-25.1**	**-24.7**	**-75.0**	**-98.3**	**-106.4**	**-115.7**	**-121.9**
CHANGE (%)		240%	152%	13%	-39%	-2%	204%	31%	8%	9%	5%
OPERATING COSTS (PER MONTH)	0.4	1.2	3.0	3.4	2.1	2.1	6.2	8.2	8.9	9.6	10.2
EBIT	**-4.2**	**-13.4**	**-32.4**	**-41.0**	**-15.1**	**-0.2**	**120.5**	**161.2**	**166.1**	**177.2**	**210.7**
CHANGE (%)		216%	141%	26%	-63%	-99%	-65446%	34%	3%	7%	19%
MARGIN (%)		-1344%	-811%		-151%	-1%	62%	62%	61%	60%	63%
EBITDA	**-4.2**	**-13.4**	**-32.4**	**-41.0**	**-15.0**	**-0.2**	**120.5**	**161.2**	**166.2**	**177.2**	**210.7**
CHANGE (%)		217%	141%	26%	-63%	-99%	-71063%	34%	3%	7%	19%
MARGIN (%)		-1343%	-810%		-150%	-1%	62%	62%	61%	60%	63%
D&A	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
NET FINANCIAL INCOME/(EXPENSES)	**-7.6**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
NET FOREIGN EXCHANGE PROFIT / (LOSS)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
PROFIT/LOSS BEFORE TAXES	**-11.9**	**-13.5**	**-32.5**	**-41.0**	**-15.1**	**-0.2**	**120.5**	**161.1**	**166.1**	**177.1**	**210.6**
CHANGE (%)		14%	141%	26%	-63%	-99%	-56730%	34%	3%	7%	19%
MARGIN (%)		-1347%	-811%		-151%	-1%	62%	62%	61%	60%	63%
TAXES	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**-7.0**	**-21.5**	**-38.8**
TAX RATE (%)	0%	0%	0%	0%	0%	0%	0%	0%	4%	12%	18%
NET PROFIT/LOSS	**-11.9**	**-13.5**	**-32.5**	**-41.0**	**-15.1**	**-0.2**	**120.5**	**161.1**	**159.1**	**155.7**	**171.9**
CHANGE (%)		14%	141%	26%	-63%	-99%	-56730%	34%	-1%	-2%	10%
MARGIN (%)		-1347%	-811%		-151%	-1%	62%	62%	58%	53%	52%
EPS (CHF)	**-0.82**	**-0.28**	**-0.67**	**-0.85**	**-0.31**	**0.00**	**2.49**	**3.34**	**3.29**	**3.22**	**3.56**
CHANGE (%)		-66%	141%	26%	-63%	-99%	-56730%	34%	-1%	-2%	10%
ESTIMATES AS OF 17 AUG 2022										SOURCE: VALUATIONLAB ESTIMATES	

NOTE:

On 31 December 2021, Spexis had a total of CHF 275 mn unrecorded tax loss carryforwards, which we anticipate the company will be able to use on future profits.

Ratios I Balance Sheet I Cash Flow Statement

SPEXIS									SHARE PRICE (CHF)	0.82
IFRS										
RATIOS	**2021**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
P/E		-2.9x	-1.2x	-1.0x	-2.6x	-186.2x	0.3x	0.2x	0.2x	0.3x	0.2x
P/S		39.6x	9.9x		4.0x	1.6x	0.2x	0.2x	0.1x	0.1x	0.1x
P/NAV		0.4x	0.5x	1.2x	2.2x	2.2x	0.3x	0.1x	0.1x	0.1x	0.1x
EV/EBITDA		-1.9x	-0.8x	-0.6x	-1.7x	-148.6x	0.2x	0.2x	0.2x	0.1x	0.1x
PER SHARE DATA (CHF)	**2021**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
EARNINGS	**-0.82**	**-0.28**	**-0.67**	**-0.85**	**-0.31**	**0.00**	**2.49**	**3.34**	**3.29**	**3.22**	**3.56**
CHANGE (%)		-66%	141%	26%	-63%	-99%	-56730%	34%	-1%	-2%	10%
CASH	**0.99**	**1.88**	**1.21**	**0.36**	**0.05**	**0.05**	**2.54**	**5.88**	**9.17**	**12.40**	**15.95**
CHANGE (%)	4254%	90%	-36%	-70%	-86%	-8%	5343%	131%	56%	35%	29%
DIVIDENDS	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
PAYOUT RATIO (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
NET ASSET VALUE	**2.08**	**2.21**	**1.54**	**0.69**	**0.38**	**0.37**	**2.87**	**6.20**	**9.50**	**12.72**	**16.28**
CHANGE (%)	-338%	6%	-30%	-55%	-45%	-1%	667%	116%	53%	34%	28%
BALANCE SHEET (CHF MN)	**2021**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
NET LIQUID FUNDS	**14.4**	**91.0**	**58.5**	**17.5**	**2.5**	**2.3**	**122.8**	**283.9**	**443.0**	**598.7**	**770.6**
TOTAL ASSETS	**49.9**	**126.4**	**94.0**	**53.0**	**37.9**	**37.7**	**158.2**	**319.4**	**478.5**	**634.2**	**806.1**
TOTAL SHAREHOLDERS' EQUITY	**30.2**	**106.8**	**74.3**	**33.3**	**18.3**	**18.1**	**138.5**	**299.7**	**458.8**	**614.5**	**786.4**
CHANGE (%)	-368%	253%	-30%	-55%	-45%	-1%	667%	116%	53%	34%	28%
RETURN ON EQUITY (%)	-39%	-13%	-44%	-123%	-83%	-1%	87%	54%	35%	25%	22%
TOTAL EQUITY	**30.2**	**106.8**	**74.3**	**33.3**	**18.3**	**18.1**	**138.5**	**299.7**	**458.8**	**614.5**	**786.4**
FINANCIAL DEBT	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
EMPLOYEES	52	30	30	31	31	31	32	32	32	32	33
CHANGE (%)	0%	-42%	1%	1%	1%	1%	1%	1%	1%	1%	1%
CASH FLOW STATEMENT (CHF MN)	**2021**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
NET PROFIT / (LOSS)	-11.9	-13.5	-32.5	-41.0	-15.1	-0.2	120.5	161.1	159.1	155.7	171.9
DEPRECIATION & AMORTIZATION	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OTHER NON-CASH ITEMS	10.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
NET CASH USED IN OPERATING ACTIVITIES	**-1.1**	**-13.5**	**-32.4**	**-41.0**	**-15.1**	**-0.2**	**120.5**	**161.1**	**159.1**	**155.7**	**171.9**
CASH FLOW FROM INVESTING ACTIVITIES	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
FREE CASH FLOW	**2.3**	**-13.5**	**-32.4**	**-41.0**	**-15.1**	**-0.2**	**120.5**	**161.1**	**159.1**	**155.7**	**171.9**
CASH FLOW FROM FINANCING ACTIVITIES	11.8	90.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CHANGE IN LIQUID FUNDS	**14.1**	**76.5**	**-32.4**	**-41.0**	**-15.1**	**-0.2**	**120.5**	**161.1**	**159.1**	**155.7**	**171.9**
ESTIMATES AS OF 17 AUG 2022									SOURCE: VALUATIONLAB ESTIMATES	

NOTE:

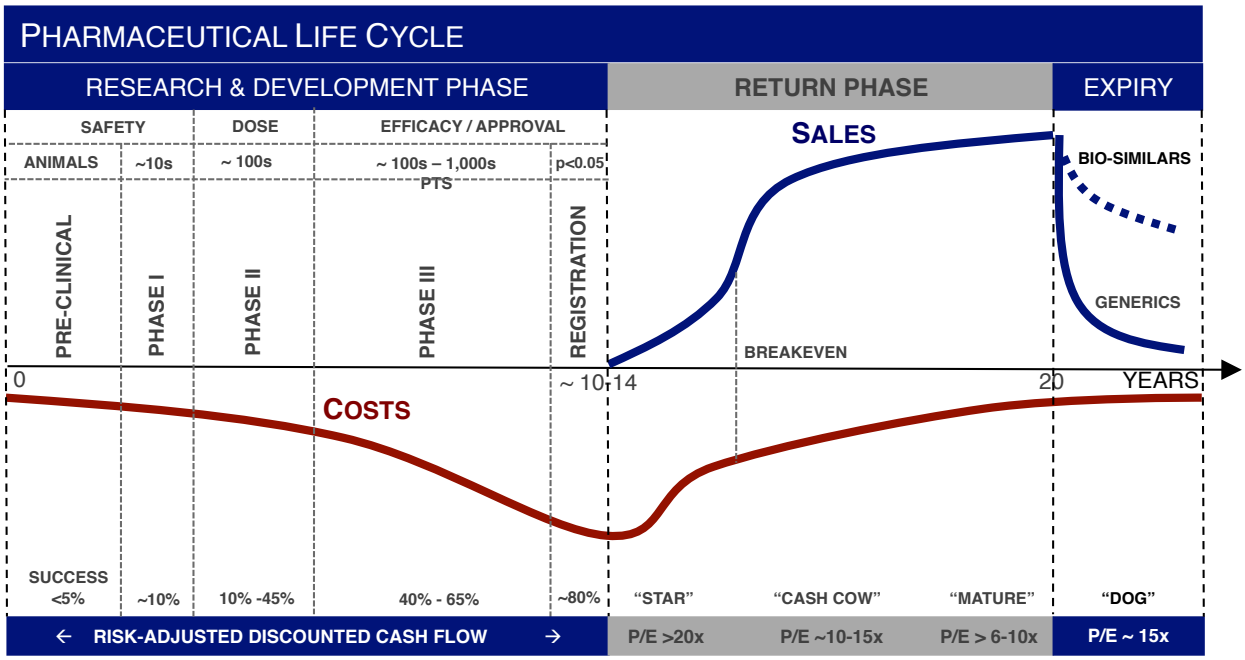
We calculate that Spexis will need a total cash injection of around CHF 90 mn to fully develop and commercialize ColiFin in the US and to fund inhaled murepavadin up to proof-of-concept (POC) in cystic fibrosis. Spexis plans to raise these additional funds in several rounds when it reaches certain key value inflection points such as the start of the "COPILOT" dosing trial (H1 2023), the start of the "COPA" phase III trial (H2 2024) of ColiFin in cystic fibrosis or on positive interim analysis "COPA" trial results (late 2024/early 2025), at far higher share prices to minimize share dilution.

Note that Spexis has other options to secure additional financing, which besides equity-based funding also includes debt financing, royalty financing, or monetizing assets such as ColiFin regional rights.

APPENDIX

Pharmaceutical life cycle

To determine the value of a prescription (bio)pharmaceutical compound, it is critical to understand its life cycle. Fortunately, all compounds follow the same life cycle. The clock starts ticking after the compound is patented, providing 20 years of protection from generic competition. Market exclusivities can extend this protection period. Additional protection is provided by orphan drug status (10 years in EU, 7 years in US). The average Research & Development Phase takes 8-14 years, leading to an effective Return Phase of 6-12 years. The Development Phase has 3 distinct Phases, focused on safety (Phase I), dose (Phase II) and efficacy/clinical benefit (Phase III). The compound is filed for registration/approval at the FDA (US) or EMA (EU). The Return Phase is characterized by a star, cash cow, and mature phase. After patent expiry (or loss of market exclusivity) generic manufacturers may copycat the branded prescription drug, at significantly lower costs, leading to a sales and earnings implosion of the branded drug.



SOURCE: VALUATIONLAB

Success Probabilities & Royalties

In our risk-adjusted NPV calculations, we use standardized success probabilities based on historical clinical success rates. The success rate increases as the project progresses through development. Sales and earnings forecasts are based on the clinical and competitive profile of the compound. The more advanced the compound is, the more accurate the forecasts become as the target market can be defined. We conservatively exclude projects that lack Phase IIa proof-of-concept data in our valuations.

SUCCESS PROBABILITIES & ROYALTIES

DEVELOPMENT STAGE	AIM	WHAT / WHO	SUCCESS PROBABILITY (%)	COSTS (USD MN)	ROYALTIES (%)
PRE-CLINICAL	SAFETY & PHARMACOLOGY DATA	LAB TESTS / ANIMALS - NO HUMANS!	< 5	3	
PHASE I	SCREENING FOR SAFETY	HEALTHY VOLUNTEERS (10'S)	5-15	3	< 5
PHASE IIA	PROOF-OF-CONCEPT	PATIENTS WITH DISEASE (10'S)	10-20		
PHASE II	ESTABLISH THE TESTING PROTOCOL	PATIENTS WITH DISEASE (100'S)	15-35	5	5-15
PHASE IIB	OPTIMAL DOSAGE	PATIENTS WITH DISEASE (100'S)	20-45	5-10	
PHASE III	EVALUATE OVERALL BENEFIT/RISK	PATIENTS WITH DISEASE (1,000'S)	40-65	> 20-1,000	10-25
REGULATORY FILING	DETERMINE PHYSICIAN LABELING	CLINICAL BENEFIT ASSESSMENT	80-90		
APPROVAL	MARKETING AUTHORIZATION	PHYSICIANS FREE TO PRESCRIBE	100		15-30

SOURCE: VALUATIONLAB, TUFTS, FDA, EMA, CLINICALTRIALS.GOV

Important Research Disclosures

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Our financial analyses are based on the "Directives on the Independence of Financial Research" issued by the Swiss Bankers Association in January 2008.

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Risk Qualification

Speculative	less than 1 year cash and breakeven beyond 1 year
High Risk	profitable within 2 years and 1 approved product/key indication (patent expiry > 5 years)
Medium Risk	profitable and/or sales from at least 2 marketed products/key indications (patent expiry > 5 years)
Low Risk	profitable and sales from >2 marketed products/key indications (patent expiry > 5 years)

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