Generating Hope for Rare Disease & Oncology Patients

November 2022
Non-Confidential
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The Spexis Proposition:
Life-changing macrocycle therapeutics for rare disease and oncology patients

**Macrocycle focus:**
- Extensive macrocycle platform with both peptidic & non-peptidic libraries
- 3 clinical-stage products discovered in-house thus far
- Lead asset ColiFin®: approved (in EU), US Phase 3-ready, also a macrocycle
- Significant molecular glue & protein degrader potential

**Early & late-stage cystic fibrosis (CF) pipeline:**
- Funded and supported by the CF Foundation & IMI

**ColiFin®:**
- Lead candidate for CF
- EU approved; U.S. Phase 3 ready
- $250M+ projected peak CF sales

**Inhaled Murepavadin:**
- 9 i.v. clinical trials in ~290 subjects to date
- Inhaled candidate in Phase 1 CF trial
- Data in Q4 2022

**Balixafortide:**
- 8 clinical trials in >500 subjects to date
- Under evaluation for possible next clinical trials

**Lonodelestat:**
- Phase 2 ready
- Out-licensed to Santhera

**Excellent value growth potential:**
- Lead asset highly de-risked
- Multiple other clinical shots-on-goal
- Cutting-edge macrocycle platform
- Company trading at significant discount to >$400M invested to date
Spexis’ Focus on Macrocycles

Broadly applicable, large clinical data set, partner validated

Macrocycles
- Can target difficult-to-drug extra- and intracellular structures
- Offer unique drug-like profiles incl. favorable PK/PD parameters, improved oral bioavailability, enhanced metabolic stability and cell permeability
- Since 2014, 19 macrocyclic structures approved by FDA

Extensive peptidic & non-peptidic libraries, databases & IP

Will fuel pipeline and generate partnering opportunities
- 2 in-house candidates progressed through P3 thus far; additional 1 (ColiFin®) in-licensed & P3-ready
- Additional candidate out-partnered & entering P2
- Validated by multiple prior pharma collaborations

1. https://doi.org/10.3390/molecules27031012
## Spexis Pipeline: Multiple “Shots-On-Goal”
### Potential for Significant Value Generation

<table>
<thead>
<tr>
<th>Program</th>
<th>Research</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Partnership / Funding</th>
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<tbody>
<tr>
<td>Cystic Fibrosis</td>
<td><strong>ColiFin</strong>&lt;sup&gt;®&lt;/sup&gt;</td>
<td>Chronic CF infections</td>
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<td><strong>OMPTA</strong></td>
<td><strong>Cystic Fibrosis Foundation</strong></td>
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<td><strong>Cystic Fibrosis Foundation</strong></td>
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<td>Oncology/Rare Disease</td>
<td><strong>Balixafortide</strong></td>
<td>Future indications under evaluation</td>
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<td><strong>OMPTA</strong></td>
<td><strong>FOSUN PHARMA</strong></td>
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<td>Neutrophil Elastase Inhibition</td>
<td><strong>Lonodelestat</strong></td>
<td><strong>CF, AATD, PCD</strong></td>
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<td><strong>santhera</strong></td>
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<tr>
<td>Macrocycle platform</td>
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<td>Broad therapeutic potential: respiratory, heme-onc/oncology, rare disease; molecular glues &amp; protein degraders</td>
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<td><strong>CARB-X</strong></td>
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- **Pipeline Today**: Indicates current phase or readiness status.
- **Readiness if/when initiated**: Indicates potential future phases or readiness.

CF – cystic fibrosis; AATD – alpha-1 antitrypsin deficiency; PCD – primary ciliary dyskinesia
ColiFin®

Already de-risked through EU approval, FDA Interactions & CF Foundation (“CFF”) support

U.S. Phase 3 Program:
- FDA “Study May Proceed Letter”: 1 Phase 3 trial sufficient
- Small 1x daily (QD) dosing cohort in Phase 3 program approved by FDA
- QD dosing favored due to high treatment burden in CF patients
- Continuous use therapy (not 28d on, 28 off): same as ColiFin® EU label
- Phase 3 developed with equity investment by CFF & significant design input from the Therapeutics Development Network – a “must have” for doing trials in the U.S. and Canada

Multiple Phase 3 value-inflection points:
- Near-term: COPilot open label safety trial to validate QD vs BID dosing
- Medium-term: COPA 4w double-blind efficacy + 20wk open label safety
- Interim readouts midway through each component of trial

Commercial:
- QIDP + Orphan Drug designation = 12 yrs U.S. market exclusivity
- Concentrated N. American market: ~130 CF care centers
- Small commercial structure sufficient to “go-it-alone”
CF Chronic Infections Promote Lung Damage Progression

Increasing Need for Inhaled Antibiotics

85% of eligible population receive CFTR modulators – slowing disease progression & improving mucus clearance¹

5yr data show reduced load BUT chronic infections persist – will remain major issue²

- Ageing CF patient population – a longer, but not healthier life¹
- Chronic lung infections – increased likelihood as patient ages; *P. aeruginosa* predominant > age 33¹
- Increasing need for long-term inhaled antibiotics¹

2) Finke et al; Lenhan et al; Quinn et al.
ColiFin®: Potential to be More Effective, Safer Therapy
Current Treatments in U.S. Not Fully Addressing Need

<table>
<thead>
<tr>
<th><strong>TOBI®/Cayston®</strong></th>
<th><strong>ColiFin®</strong></th>
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<tbody>
<tr>
<td><strong>Mechanism of Action</strong></td>
<td>Leads to resistance development</td>
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<tr>
<td><strong>Resistance Development</strong></td>
<td>Increasing, up to 40% in some regions(^1,2)</td>
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<td><strong>Safety</strong></td>
<td>TOBI has significant ototoxicity concerns</td>
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<td><strong>Efficacy</strong></td>
<td>Decreased efficacy over time</td>
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<tr>
<td><strong>Dosing</strong></td>
<td>Continuous b.i.d./t.i.d. alternating therapy (“CAT”) (rotation of 28d cycles)</td>
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**U.S. prices typically higher than in Europe – ColiFin® can be priced 5-8x higher than in EU, in line with competitive products in U.S.**

<table>
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<th><strong>28d AWP Pricing</strong></th>
<th><strong>ColiFin®</strong></th>
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<td>Between ~$5,400 – 11,000 (generics – branded)</td>
<td>Targeting ~$8,000</td>
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*Colistin available as I.V. formulation – inhalation unapproved (U.S.) → not reimbursed, most patients must pay-out-of-pocket*

1) doi: 10.1128/AAC.01541-19
2) doi: 10.1128/AAC.02483-20
ColiFin® Phase 3 Program: COPILLOT Trial

Primary Objective:
- Tolerability and safety of ColiFin®, once-daily (QD) vs twice-daily (BID)
- Interim analysis (Day 42) to support switch from BID to QD dosing in COPA
- Important short-term value inflection point: QD approval could grant USP

Secondary Objectives:
- Assessment of pulmonary function (ppFEV1)
- Clinical events (number/severity of pulmonary exacerbations, hospitalizations)
- Additional antibacterial therapy

To be conducted in Europe; enrollment expected to initiate 1H2023

Screening:
Patients on stable inhaled antibiotic treatment

<table>
<thead>
<tr>
<th>D1: 1:1 randomization QD vs. BID*</th>
<th>D 28: End of treatment</th>
<th>D 42: Interim analysis</th>
<th>D 169: End of trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>ColiFin® 4 MIU QD, n=19</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ColiFin® 2 MIU BID, n=19</td>
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20 wk follow-up on “usual care”

* Stratification by current use of oral corticosteroids > or <= 10 mg QD or 20 mg QOD (prednisone or prednisolone equivalents)
**ColiFin® Phase 3 Program: COPA Pivotal Trial**

28d double blind efficacy + 20w open-label safety

**Screening:**
Patients on tobramycin, aztreonam or levofloxacin

**Eligible:** Adults/adolescents with CF + chronic *P. aeruginosa (Pae)* lung infection

**Therapy:** Continuous ColiFin® for 6 months vs. placebo + usual inhaled antibiotics

**Primary endpoint:** Mean absolute diff. in ppFEV1** (of ≥3 %) in change from baseline to Day 28

**Key secondary endpoints throughout 6 months:** Difference in CFQ-R respiratory symptom score; exacerbation severity/duration; consistency of treatment response; sputum microbiology: *Pae* density, resistance development (MIC)

**Independent Data Monitoring Committee:** Interim efficacy analysis after 288 patients complete 28d days of treatment (~12 mos from FPI)

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**Part A: 28d double-blind efficacy**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ColiFin®</td>
<td>360</td>
<td>Rollover from ColiFin group; total n=300 completed</td>
</tr>
<tr>
<td>Placebo</td>
<td>120</td>
<td>Rollover from placebo group; total n=100 completed</td>
</tr>
</tbody>
</table>

**Part B: 20wk open label safety**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>ColiFin® QD</td>
<td></td>
<td>Active Control (&quot;usual care&quot;) Rollover from placebo group; total n=100 completed</td>
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</table>

**Timeline:**

- **D 1:** 3:1 randomization*
- **D 28:** Roll over
- **D 169:** End of trial
- **D 199:** Safety follow-up (tel.); End of trial

* Stratification of randomization by age (<18, ≥18 yrs, ≤70% ≥70%), prior PEx treated with systemic antibacterials in last 12 months, stable baseline use of CFTR modulators

** ppFEV1: Percent Predicted Forced Expiratory Volume in 1 second
Future ColiFin® Patients
Already Use Inhaled Colistin

Current EU Usage
- EU inhaled colistin revenues (all products) estimated €75M/yr
- Average EU price per course: €800-1.5K[1]

Current US Usage
- ~3600 CF patients use unapproved colistin[2]
- Those patients will convert to ColiFin® upon approval[3]

EU vs. US
- US pricing 3-5x EU (per TOBI®, Cayston®, generics)
- EU29 & US CF patient population comparable (~40K vs 30K)

[1] Confidential market information shared
Non-CF Bronchiectasis & COPD patients also suffer chronic *P. aeruginosa* infections, no proven inhaled standard-of-care.

An effective QD ColiFin® would be an attractive therapeutic in both these additional indications.

**ColiFin® Life Cycle Management:**

**Expansion into Non-CFBE, COPD**

1. **Cystic Fibrosis**
   - ~10K Treatable US Patients
   - Primary indication w/ front-line label
   - Very accessible patient population
   - Established usage in U.S. & RoW

2. **Non-CF Bronchiectasis**
   - 15x U.S. CF Market
   - 1/3rd of patients have 3+ exacerbations/yr
   - Most of these have chronic lung infections
   - ~30% culture *P. aeru*, have worse outcomes

3. **COPD**
   - 50x U.S. CF Market
   - 15M US Patients, >250M globally
   - 5-15% of patients infected with *P. aeru*
   - Infections drive exacerbations, deaths

**LCM Expands Treatable Patients to >30M Worldwide**

- 15M US Patients, >250M globally
- 5-15% of patients infected with *P. aeru*
- Infections drive exacerbations, deaths
### Inhaled Murepavadin ("iMPV") for Cystic Fibrosis

#### Novel Class Therapeutic For a Rare Disease

#### Attractive market
- Peak CF sales 200-400m USD
- Label expansion potential to nCFBE: >$1B market

#### In Phase 1
- Potent & selective activity against resistant *P. aeruginosa*

#### Externally validated & partially funded
- Clinical development externally with substantial funding from: EU Innovative Medicines Initiative (IMI) for Ph. 1a & CF Foundation for Ph. 2

#### High safety margin
- 9 clinical trials of IV MPV totaling 290 subjects have informed & de-risked the inhalation route
- Low systemic exposure upon inhalation mitigates nephrotoxicity risk
- High safety margin (5- to 10-fold above IV) in GLP tox studies

#### IP protected
- Market exclusivity through about 2036 via COM/additional IP
- Eligible for QIDP & orphan drug status

### Timeline

<table>
<thead>
<tr>
<th>2021</th>
<th>2022</th>
<th>2023</th>
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<tr>
<td>Ph 1a: SAD in HVs</td>
<td>Ph 1b: SAD in CF</td>
<td>Ph 2: CF patients</td>
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</table>
Balixafortide: Potent CXCR4 inhibitor

Applicable to wide range of oncology and rare disease indications

Balixafortide
• Potent, highly selective blocker of CXCR4
• CXCR4 is involved in tumor growth and metastasis and is also implicated in a variety of primary immune deficiency and other rare diseases

Clinical proof of concept established
• >500 patients in 8 clinical trials
• Phase 3 study in advanced HER-2 negative breast cancer did not achieve primary endpoint; data analyses ongoing

Good safety and tolerability profile
• Well tolerated by i.v. route of administration
• No limiting safety events identified at top dose given (5.5mg/kg)
• Shown to overcome SoC drug resistance
• Compatible with combination therapies

Evaluating potential new indications
• Extensively profiled in animal models of stem cell mobilization, cancer, inflammatory and rare disease indications
• Synergistic efficacy in combination with docetaxel compared to either drug alone in metastatic prostate cancer model
• Other studies/analyses ongoing and to be reported on ASAP
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<thead>
<tr>
<th>Name</th>
<th>Role</th>
<th>Experience Details</th>
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<tbody>
<tr>
<td>Jeff Wager, MD</td>
<td>CEO &amp; Chairman</td>
<td>30 yrs VC &amp; CEO leadership; &gt;$2.5B in value created since 2000</td>
</tr>
<tr>
<td>Hernan Levett</td>
<td>CFO</td>
<td>25+ yrs financial leadership in pharma / biotech</td>
</tr>
<tr>
<td>Juergen Froehlich, MD</td>
<td>CMO</td>
<td>30+ yrs Chief Medical Officer &amp; senior reg affairs experience</td>
</tr>
<tr>
<td>Stephan Wehselau</td>
<td>COO &amp; President</td>
<td>20+ yrs CEO &amp; CFO experience, ~$400M raised in career</td>
</tr>
<tr>
<td>Dennis Ausiello, MD</td>
<td>Vice Chair of the Board</td>
<td>17yrs Physician-in-Chief, MGH 8 yrs lead director of the Pfizer board</td>
</tr>
<tr>
<td>Kuno Sommer, PhD</td>
<td>Director</td>
<td>Former CEO, Berna Biotech (acq. by J&amp;J) Chairman Bachem, Sunstar, Targimmune, more</td>
</tr>
<tr>
<td>Robert Clarke, PhD</td>
<td>Director</td>
<td>20+ yrs inhaled R &amp; D and CEO experience</td>
</tr>
<tr>
<td>Dan Hartman, MD</td>
<td>Director</td>
<td>25+yrs R &amp; D leadership; Head of $2B Gates malaria R &amp; D portfolio</td>
</tr>
<tr>
<td>Bernard Bollag, MBA</td>
<td>Director</td>
<td>Senior finance executive across corporate finance &amp; capital markets</td>
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Spexis

Near-term and multiple value inflection points

CF therapeutic proposition addresses important and growing need

Two CF clinical candidates
- ColiFin® – starting Phase 3 1H2023
- Inhaled murepavadin (iMPV) – Phase 1 ongoing with first data expected (Q4-22)

Balixafortide (BLX)
- 8 clinical trials to date; >500 subjects dosed; under evaluation for additional oncology & rare disease indications

Proprietary macrocycle platform poised to build pipeline and fuel corporate partnerships
- Result of >$400M prior investment & multiple alliances
- iMPV, BLX & lonodelestat generated by our macrocycle platform; ColiFin® (in-licensed from PARI) also a macrocycle
- Highly leverageable towards other extracellular, intracellular & protein-protein interaction targets
- Ideal for targeting protein-protein interactions, molecular glues and targeted therapies
Thank you!

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<td><strong>Website link</strong></td>
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<td><strong>IR email</strong></td>
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