Scaling Mobile/Digital Technologies to Objectively Measure Pain Associated with Endometriosis

New Clinical Trial Results and Progress

Jiao Li – Digital Technology Lead
CHUGAI PHARMACEUTICAL

Jaydev Thakkar – Chief Operating Officer
BIOFOURMIS
Key Takeaways

Plan for the lifetime value of investment in digital biomarkers

Understand the scientific rigor needed to achieve clinical AND commercial outcomes

Focus on patient engagement and simplicity to drive adherence
Optimizing Drug Lifecycle Value

Co-Development → SaMD | Digital Companions | Digital Biomarkers

**Early-Stage Candidates**
- Precision medicine that uses biomarkers and AI/ML tools. Allows dose titration and optimization personalized for each patient.
- Early evidence to advance promising candidates, or “fail fast” unsuitable ones
- Differentiation through SaMD development

**Mid/Late-stage Candidates**
- Patient-centric digital biomarkers as surrogate endpoints to speed clinical development
- Remote/home monitoring for enhanced patient experience and access to diverse population
- Biosensor data for improved assessment of efficiency, side effects, and outcomes

**Marketed Drugs**
- Leverage integrated networks of health system partners to find therapy candidates and drive commercial outcomes
- Integration into disease-specific dynamic care pathways to optimize care delivery
- Observational data and surveillance to help FDA post-market drug safety monitoring

© 2023 Biofourmis Inc. and Chugai Pharmaceutical Co, Ltd. All rights reserved.
Endometriosis and AMY109

Chugai is developing a new drug AMY109 to treat endometriosis. The most common symptom of endometriosis is pelvic pain.

Endometriosis:
1 in 10 reproductive age women

AMY109 Anti-IL-8 recycling antibody:
- A non-hormonal, disease modifying drug to reduce pain and improve Quality of Life of endometriosis patients
- Current phase: P1
- Mechanism of Action: Anti IL-8 humanized monoclonal antibody

Figure reference: ESHRE Guideline Endometriosis (https://www.eshre.eu/Guideline/Endometriosis)
Challenge in Pain Measurement

Precisely assessing drug efficacy using traditional pain measurements like patient reported outcomes (PRO) due to limited snapshot data.

**CURRENT STATE**
- Snapshot data (PRO)
- No difference between Active and Placebo

**FUTURE STATE**
- Continuous data (Sensor)
- Difference by time-course data
Technology Selection

Purpose: Continuously and objectively measure pain intensity in endometriosis patients

Causes of endometriosis-associated pain\textsuperscript{1,2}: Autonomic Nerve System (ANS)

Vitals related to pain caused by ANS: Heart Rate Variability, Skin Conductance

Clinical Observational Study - Methods

We conducted a study to assess the feasibility of Biofourmis’ Biovitals Pain Index™ that uses biometric parameters from a wearable sensor and mobile platform to continuously measure pain in endometriosis patients.

Study Design
- A 12-week, single-arm observational study
- 7 sites in the US, Singapore, and Taiwan

Data Collection
- Wearable: >15 hours/day
- Pain report: 3 times/day + ad-hoc
- Quality of Life report: weekly, monthly

E4®
Femme Rhythm™ app

Continuous compliance tracking – need based telephone follow up

E4 figure reference: https://www.empatica.com/research/e4/
Clinical Observational Study - Patient Engagement

To engage patient, we combined multiple techniques in app and operation design. We got relatively good compliance rate of device and patient reported outcomes.

App and operation design
- Large data plan for BYOD → Provisioned phone
- Notification, encourage message, gamification, award
- User training, helpdesk
- User survey for future design improvement

Compliance rate and Patient experience
- Device: > 50% patients compliance rate 50%+
- Pain Report: >80% patients compliance rate 75%+

E4®
Femme Rhythm™ app

Remote Home Monitoring
Continuous compliance tracking – need based telephone follow up

E4 figure reference: https://www.empatica.com/research/e4/
Clinical Observational Study – Results (1/3)

**PATIENT DISPOSITION**

### Patient Diagram

- 90 subjects Enrolled
- Analyzed N=86

**Discontinued (N=9)**
- Non-compliance (N=5)
- Loss to follow-up(N=1)*
- Not fulfilling Inclusion criteria(N=3)*

*Excluded from analysis

### Summary of Pain Reports for 86 Eligible Patients

<table>
<thead>
<tr>
<th>Pain Categories (by NRS)</th>
<th>All pain reports</th>
<th>Endometriosis-related pain reports</th>
<th>Valid Endometriosis-related pain reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = None</td>
<td>16,577 (69.0%)</td>
<td>16,558 (74.0%)</td>
<td>15,384 (74.7%)</td>
</tr>
<tr>
<td>1-3 = Mild</td>
<td>4,519 (18.8%)</td>
<td>3,518 (15.7%)</td>
<td>3,256 (15.8%)</td>
</tr>
<tr>
<td>4-6 = Moderate</td>
<td>1,695 (7.0%)</td>
<td>1,288 (5.8%)</td>
<td>1,114 (5.4%)</td>
</tr>
<tr>
<td>7-10 = Severe</td>
<td>1,242 (5.2%)</td>
<td>999 (4.5%)</td>
<td>852 (4.1%)</td>
</tr>
<tr>
<td>NA</td>
<td>1 (0.0%)</td>
<td>1 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>24,584</td>
<td>22,364</td>
<td>20,606</td>
</tr>
</tbody>
</table>

### Age on enrollment
- mean (min-max) year: 37.9(22-48)

### Ethnicity
- Chinese: 58 (67.5%)
- Malay: 10 (11.6%)
- Indian: 8 (9.3%)
- White American: 8 (9.3%)
- Others: 2 (2.3%)

### Severity of pain
- Moderate: 71 (82.6%)
- Severe: 15 (17.4%)

### Illness duration (years)
- < 5: 69 (80.2%)
- 5 – 10: 13 (15.1%)
- > 10: 4 (4.7%)

### Type of lesion
- Ovarian cyst: 49 (57.0%)
- Deep infiltrating endometriosis: 13 (15.1%)
- Superficial lesion: 12 (14.0%)
- Adenomyosis: 39 (45.3%)
- Adhesion: 12 (14.0%)
- Others: 8 (9.3%)
Clinical Observational Study – Results (2/3)

Pain Index vs. Numerical Rating Scale (NRS) score for a specific patient in 3 months
Clinical Observational Study – Results (3/3)

Primary Endpoint: Concordance between Numerical Rating Scale (NRS) score and Biovitals Pain Index™

<table>
<thead>
<tr>
<th>Pain Index</th>
<th>None (0)</th>
<th>Mild (1-3)</th>
<th>Moderate (4-6)</th>
<th>Severe (7-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>15,077</td>
<td>908</td>
<td>330</td>
<td>98</td>
</tr>
<tr>
<td>Mild</td>
<td>238</td>
<td>2,168</td>
<td>195</td>
<td>29</td>
</tr>
<tr>
<td>Moderate</td>
<td>50</td>
<td>156</td>
<td>868</td>
<td>82</td>
</tr>
<tr>
<td>Severe</td>
<td>19</td>
<td>24</td>
<td>50</td>
<td>314</td>
</tr>
</tbody>
</table>

The Cohen's Kappa was 0.72 (95% CI 0.71-0.73) for concordance between Pain Index and NRS. The Pain Index correctly predicted in 98.0% (n=15,077) of none pain, 66.6% (n=2,168) of mild pain, 60.2% (n=868) of moderate pain, and 60.0% (n=314) of severe pain.
Clinical Observational Study

Outcome and Next Steps

- The Biovitals Pain Index™ demonstrates the potential to correctly measure endometriosis related pain.
- The Biovitals Pain Index™ was generated from physiological data and individual’s baseline information, meaning less prone to report biases from patients.
- Further investigation is required to analyze and characterize the patient population for which this would be most optimal.
- Objective pain assessment by wearable device and mobile app might be supportive to endometriosis diagnosis and could contribute to endometriosis management.
Next Step

Chugai and Biofourmis entered into new partnership focused on data-driven virtual care for endometriosis-related pain

The collaboration focuses on

- Improve the pain measurement technology for endometriosis
- Develop a virtual care platform to enable real-world data-driven pain measurement
- Deliver virtual specialty care to endometriosis patients in the U.S.
- Generate insight from the data collected from the platform to support Chugai’s R&D and post-marketing activities on endometriosis

Thank you