Safe Harbor

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Key Financial Highlights

Market Cap at 06.05.2017 Mn CHF: **2'454.12**
Number of shares: **15’037’483**
Listing: SIX Swiss exchange, Main board

KEY FIGURES 2016 in EUR Mn:
Revenues: **67.664**
EBT: **27.491**
Net Profit: **19.340**

Liquidity at 5.19.2017: **306.683**
Equity Ratio at 5.19.2017: **94%**
Total Equity: **415.558**
Total Assets: **443.474**
Cosmo: an established leader in GI
Cumulative 2016 Sales of approved products in USD Mn: 947.1

In USD Mn, 2016: 792.1

In USD Mn, 2016: 155
Cosmo: expanding the GI franchise beyond Lialda and Uceris capturing full value
Cosmo: expanding in the Endoscopy franchise

[Logos of LuMeBlue, Eleview™, and Remimazolam]
Expanding the GI Franchise
Zemcolo’s API is Rifamycin SV, a well established, broad spectrum, orally non-absorbable, low toxicity, semi-synthetic, antibiotic, approved and marketed for parenteral or topical use in some EU Countries for systemic or local infections control.

Zemcolo’s oral administration does not cause appreciable blood serum levels in the systemic circulation: this makes the drug an ideal agent for the treatment of colonic infections.

Cosmo’s technology allows the antibiotic to be delivered directly into the colon, avoiding unwanted effects on bacterial flora residing in the upper portions of the gastrointestinal tract.
Zemcolo in a nutshell

Zemcolo provides an effective and innovative treatment option for colonic infections:

- significantly reduces TLUS in Traveller’s Diarrhea
- showed non-inferiority vs Xifaxan in TLUS and treatment success rates in a randomized, double-blind phase II clinical trial
- TLUS was significantly shorter in Zemcolo compared to placebo in a randomized, double-blind phase III clinical trial
- showed non-inferiority in terms of TLUS and similar efficacy, compared to Ciprofloxacin in a randomized, double-blind phase III clinical trial

Zemcolo has a negligible systemic absorption (not higher than 0.0036% of the dose). Thus it minimizes systemic side effects and clinically significant drug interactions as well as potential sequelae from antibiotic use, including overgrowth of pathogenic bacteria (i.e. C. diff) and opportunistic infections (i.e. Candida).

Zemcolo is a New Chemical Entity (NCE) in the US and will, upon approval, enjoy 10 years of exclusivity in USA under the NCE/GAIN Act combined rules.
Zemcolo has undergone two successful Pivotal Clinical Trials

1. **US TRIAL (SUPERIORITY VS. PLACEBO)** A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Zemcolo for the Treatment of Travelers' Diarrhea.

2. **EU TRIAL (NON-INFERIORITY VS. CIPRO)** A randomized, double-blind, double-dummy, multi-center, comparative parallel-group study to evaluate the efficacy and safety of oral daily Zemcolo 400 mg b.i.d. vs. Ciprofloxacin 500 mg b.i.d. in the treatment of acute infectious diarrhea in travelers.
Zemcolo: TD trials
Non-inferiority vs Cipro (standard of care) (Falk) Outcome

Non-inferiority of Zemcolo vs Ciprofloxacin in main microbial strain reduction upon treatment

<table>
<thead>
<tr>
<th>Microbial Strain</th>
<th>Baseline</th>
<th>Final</th>
<th>% reduct.</th>
<th>Baseline</th>
<th>Final</th>
<th>% reduct.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giardia lamblia</td>
<td>45</td>
<td>19</td>
<td>57.8</td>
<td>34</td>
<td>15</td>
<td>55.9</td>
</tr>
<tr>
<td>Cryptosporidium parum</td>
<td>14</td>
<td>1</td>
<td>92.9</td>
<td>6</td>
<td>1</td>
<td>83.3</td>
</tr>
<tr>
<td>E. Hystolytica</td>
<td>0</td>
<td>0</td>
<td>100.0</td>
<td>0</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td>Shigella group</td>
<td>9</td>
<td>1</td>
<td>88.9</td>
<td>6</td>
<td>1</td>
<td>83.3</td>
</tr>
<tr>
<td>Salmonella group</td>
<td>5</td>
<td>0</td>
<td>100.0</td>
<td>11</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td>Campylobacter Jejuni</td>
<td>16</td>
<td>2</td>
<td>87.5</td>
<td>24</td>
<td>7</td>
<td>70.8</td>
</tr>
<tr>
<td>Aeromonas</td>
<td>7</td>
<td>2</td>
<td>71.4</td>
<td>9</td>
<td>1</td>
<td>88.9</td>
</tr>
<tr>
<td>Plesiomonas</td>
<td>4</td>
<td>1</td>
<td>75.0</td>
<td>3</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td>Heat stable toxin (ST)</td>
<td>127</td>
<td>55</td>
<td>56.7</td>
<td>128</td>
<td>53</td>
<td>58.6</td>
</tr>
<tr>
<td>Heat Labile toxin (LT)</td>
<td>16</td>
<td>6</td>
<td>62.5</td>
<td>11</td>
<td>7</td>
<td>36.4</td>
</tr>
<tr>
<td>Heat stable/lable toxin (SLT)</td>
<td>16</td>
<td>5</td>
<td>68.8</td>
<td>9</td>
<td>3</td>
<td>66.7</td>
</tr>
<tr>
<td>E. Coli enteroaggregative</td>
<td>99</td>
<td>22</td>
<td>77.8</td>
<td>89</td>
<td>23</td>
<td>74.2</td>
</tr>
<tr>
<td>Norovirus</td>
<td>9</td>
<td>1</td>
<td>88.9</td>
<td>12</td>
<td>4</td>
<td>66.7</td>
</tr>
<tr>
<td>totali</td>
<td>367</td>
<td>115</td>
<td>68.7</td>
<td>345</td>
<td>115</td>
<td>66.7</td>
</tr>
</tbody>
</table>
**Zemcolo: TD trials**  
**Superiority vs placebo (Santarus)**  

Microbiological Eradication by Pathogen (Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Placebo (N=65) No. of Isolates</th>
<th>Ryfamicin – MMX (N=199) No. of Isolates</th>
<th>Percent Eradication</th>
<th>Percent Eradication</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All pathogens</td>
<td>62</td>
<td>185</td>
<td>28</td>
<td>61</td>
<td>0.0836</td>
</tr>
<tr>
<td>Invasive Group</td>
<td>13</td>
<td>24</td>
<td>7</td>
<td>8</td>
<td>0.2250</td>
</tr>
<tr>
<td>Campylobacter jejuni</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0.3496</td>
</tr>
<tr>
<td>Shigella group</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>NC</td>
</tr>
<tr>
<td>Salmonella group</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0.1360</td>
</tr>
<tr>
<td>Plesiomonas group</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>NC</td>
</tr>
<tr>
<td>Vibrio group</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>NC</td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>NC</td>
</tr>
<tr>
<td>Entamoeba histolytica</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>NC</td>
</tr>
<tr>
<td>Cryptosporidium parvum</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0.2850</td>
</tr>
<tr>
<td>Norovirus</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>0.3613</td>
</tr>
</tbody>
</table>

*Note: NC indicates not calculable.*
Zemcolo: in vitro  
Activity against various gastroenteritis pathogens

<table>
<thead>
<tr>
<th>Bacterial Strain</th>
<th>MIC (µg/mL)</th>
<th>MBC (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli ATCC 25922</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>E. cloacae ATCC 13047</td>
<td>64</td>
<td>64</td>
</tr>
<tr>
<td>P. mirabilis ATCC 12453</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>S. sonnei ATCC 25931</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>S. typhimurium ATCC 13311</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Y. enterocolitica ATCC 9610</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>E. faecium ATCC 6559</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>E. fecalis ATCC 29212</td>
<td>0.125</td>
<td>0.125</td>
</tr>
<tr>
<td>S. epidermidis</td>
<td>0.125</td>
<td>0.125</td>
</tr>
<tr>
<td>N. gonorrhoeae ATCC 19424</td>
<td>0.125</td>
<td>0.125</td>
</tr>
<tr>
<td>C. difficile ATCC 43593</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>S. aureus ATCC 29213</td>
<td>0.004</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Source: Gismondo, Report 19-Nov-07
Rifamycin SV shows a clear-cut in vitro efficacy against pathogens associated with TD.

### Zemcolo: in vitro Activity against Escherichia coli and invasive bacteria

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>All strains (443)</td>
<td>32</td>
<td>128</td>
<td>2 - &gt;512</td>
</tr>
<tr>
<td>EHED (105 strains)</td>
<td>32</td>
<td>64</td>
<td>8 - 256</td>
</tr>
<tr>
<td>ETEC (201 strains)</td>
<td>64</td>
<td>128</td>
<td>2 - &gt;512</td>
</tr>
<tr>
<td>EPEC (45 strains)</td>
<td>64</td>
<td>128</td>
<td>16 - 128</td>
</tr>
<tr>
<td>EAEC (92 strains)</td>
<td>32</td>
<td>128</td>
<td>4 - 256</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibrio parahaemolyticus (42 strains)</td>
<td>2</td>
<td>2</td>
<td>2 - 4</td>
</tr>
<tr>
<td>Plesiomonas shigelloides (16 strains)</td>
<td>8</td>
<td>8</td>
<td>4 - 8</td>
</tr>
<tr>
<td>Aeromonas hydrophila (101 strains)</td>
<td>4</td>
<td>16</td>
<td>2 - 512</td>
</tr>
<tr>
<td>Shigella spp. (105 strains)</td>
<td>32</td>
<td>64</td>
<td>8 - 128</td>
</tr>
<tr>
<td>Salmonella spp. (102 strains)</td>
<td>128</td>
<td>256</td>
<td>16 - 256</td>
</tr>
<tr>
<td>Campylobacter spp. (102 strains)</td>
<td>&gt;512</td>
<td>&gt;512</td>
<td>&gt;512</td>
</tr>
</tbody>
</table>
Two successful Pivotal Clinical Trials

Zemcolo shows a TLUS clearly shorter than placebo

Zemcolo is as efficacious as Cipro in treating TD patients and clearly superior to placebo

<table>
<thead>
<tr>
<th>Falk</th>
<th>Santarus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>Rifamycin SV-MMX</td>
</tr>
<tr>
<td>(FAS n=415)</td>
<td>(FAS=420)</td>
</tr>
<tr>
<td>Placebo</td>
<td>Rifamycin SV-MMX</td>
</tr>
<tr>
<td>(ITT n=65)</td>
<td>(ITT n=199)</td>
</tr>
<tr>
<td>352 (84.8%)</td>
<td>357 (85%)</td>
</tr>
<tr>
<td></td>
<td>37 (56.9%)</td>
</tr>
<tr>
<td></td>
<td>162 (81.4%)</td>
</tr>
</tbody>
</table>

Non-inferiority vs Cipro (standard of care) (Falk) Outcome
Significant edge against competitors

Xifaxan

Compared to Xifaxan, Zemcolo allows antibiotic to be delivered directly to the colon, avoiding unwanted effects on the beneficial saprophytic bacterial flora living in the upper portions of the gastrointestinal tract; and it enjoys significantly more potent anti-inflammatory properties.

Ciprofloxacin

Compared to Ciprofloxacin, Zemcolo has no systemic absorption (very important for resistance) and no warning box issues, thus being way safer in the same context.
When corrected for number of viable cells, it is shown that Zemcolo is a more potent anti-inflammatory agent than Xifaxan in macrophages and colonic cell lines.
Based on the EC50 values, Rifamycin SV is 100 times more potent than Rifampicin.

Rifamycin SV is at least 1000 times more potent than Rifaximin at stimulating PXR transcriptional activity in a cell line engineered to express a fusion human PXR protein.

In terms of the maximum possible stimulation of PXR activity, Rifaximin at 30 µM only activates up to 60% of the maximum activity with Rifamycin SV at 0.3 µM.
Zemcolo Development Plan

US (Cosmo/Aries)
File NDA for TD in H1 2017
Extend indication to: IBS D
Development Timeline: Phase II DR in EU to start in H1 17

EU (licensed to Dr. Falk)
File NDA for TD in H1 2017
Extend indication to: Uncomplicated Diverticulitis
Development Timeline: Phase II P.O.C. ongoing interim analysis in June 2017
Exploiting the Colonoscopy mass market becoming a one-stop shop

- Improve Lesion Detection
- Improve Lesion Removal
- Improve Procedure Efficiency

- LuMeBlue
- Eleview™
- Remimazolam
Exploiting the colonoscopy mass market

<table>
<thead>
<tr>
<th>Description</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of colonoscopies in USA 2017</td>
<td>16’000’000</td>
</tr>
<tr>
<td>Number of colonoscopies in EU 2017</td>
<td>17’000’000</td>
</tr>
<tr>
<td>Potential for the RoW</td>
<td>60’000’000</td>
</tr>
</tbody>
</table>
Improve Lesion Removal
Ideal Submucosal Injectable Lifting Agent

- Designed to lower risk of perforation
  - Helps to visualize margins of the target lesion
  - Improved margin visualization helps decrease risk of damage to the external muscular layer, which could lead to perforation

- Designed for efficiency
  - Designed to decrease time needed to completely resect a lesion
  - Reduces reinjections required and piecemeal excisions compared to saline

- Requires less volume to create cushions
  - Less volume required to create submucosal cushions compared to normal saline better cushion-forming ability than saline
  - Maintains cushions without releasing liquid after resection 54% less is required to maintain a cushion in ESDs

- Safety and tolerability profile comparable to saline
  - No differences were reported in minor and major adverse events in a randomized trial
Unique & Novel Mechanism

Upon injection:

Eleview™: Reconfigures to form a colored cushion\(^1\)
Creates an “artificial net” formed by polymer chains\(^2\)
Traps water within to build a colored cushion of optimal shape, height, and duration\(^1\)

---

1 Eleview™ Instructions for use, Aries Pharmaceuticals, Inc. April 2017
2 Data on File, Aries Pharmaceuticals, Inc.
The current standard:
a hand-made saline solution application
See the difference with Eleview™

Image 2016 (Milan, Italy)

Live endoscopic session

Removal of a granular type lateral spreading lesion (LST)

Selected technique: EMR

Endoscopist: Dr. Pradeep Bhandari (UK)
Eleview™ has just successfully completed a clinical trial showing superiority vs the standard saline solution in all endpoints.
All primary endpoints were in favour of Eleview™

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Statistics</th>
<th>Eleview™ (N=102) (n=102)</th>
<th>Reference Comparator (N=109) (n=110)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to resect the lesion</td>
<td>Mean (±SD)</td>
<td>16.1 (± 9.8)</td>
<td>31.6 (±32.1)</td>
</tr>
<tr>
<td></td>
<td>Range (min-max)</td>
<td>3.0 – 41.0</td>
<td>4.0 - 248.0</td>
</tr>
<tr>
<td></td>
<td>𝑃 value</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Total injected volume per lesion size (mL/mm)</td>
<td>Mean (±SD)</td>
<td>0.53 (± 0.32)</td>
<td>0.92 (±0.65)</td>
</tr>
<tr>
<td></td>
<td>Range (min-max)</td>
<td>0.00 – 1.75</td>
<td>0.20 – 4.96</td>
</tr>
<tr>
<td></td>
<td>𝑃 value</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>
All primary endpoints were in favour of Eleview™ (CONTD)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Statistics</th>
<th>Eleview™ (N=102) (n=102)</th>
<th>Reference Comparator (N=109) (n=110)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to resect the lesion (minutes)</td>
<td>Mean (±SD)</td>
<td>19.15 (±16.80)</td>
<td>29.70 (±69.18)</td>
</tr>
<tr>
<td></td>
<td>Range (min-max)</td>
<td>1-100</td>
<td>2-687</td>
</tr>
<tr>
<td></td>
<td>% difference⁸</td>
<td>-35.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.326</td>
<td></td>
</tr>
</tbody>
</table>

⁸Eleview™ vs reference comparator.

- This can be attributed to the high variability of data, particularly in the reference comparator arm (SD Eleview™ = 16.80 m; SD reference comparator =69.18 m → 4 times increase)

- Nevertheless, it is evident that there is a positive trend toward a reduction of the time needed to complete the procedure using Eleview™ with respect to comparator: reduction of 35.5% (10.6 minutes/procedure). This trend is confirmed by the whole colonoscopy time (one of the secondary end points)
All secondary endpoints were in favor of Eleview™

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Statistics</th>
<th>Eleview™ (N=102) (n=102)</th>
<th>Reference Comparator Eleview™ n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sidney Resection Quotient (SRQ)</td>
<td>Mean (±SD)</td>
<td>10.3 (±8.1)</td>
<td>8.0 (±5.7)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td>Number of resection pieces</td>
<td>Mean (±SD)</td>
<td>5.70 (6.0%)</td>
<td>6.47 (5.0%)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.052</td>
<td></td>
</tr>
<tr>
<td>Injected volume to provide initial lift (mL)</td>
<td>Mean (±SD)</td>
<td>10.4 (±7.0)</td>
<td>15.3 (±11.7)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Proportion of subjects with en bloc resections</td>
<td>Mean (±SD)</td>
<td>19 (18.6%)</td>
<td>12 (11.0%)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.125</td>
<td></td>
</tr>
</tbody>
</table>
Eleview is as safe as the standard saline solution

<table>
<thead>
<tr>
<th>Complication</th>
<th>Eleview™ n (%)</th>
<th>Reference Comparator Eleview™ n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject with at least one complication</td>
<td>17 (15.0)</td>
<td>17 (15.2)</td>
</tr>
<tr>
<td>Intraprocedural bleeding</td>
<td>8 (7.1)</td>
<td>11 (9.8)</td>
</tr>
<tr>
<td>Early (&lt;24h) bleeding</td>
<td>2 (1.8)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Delay bleeding (≥24h post EMR)</td>
<td>0 (0.0)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Perforation</td>
<td>0 (0.0)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Postpolypectomy syndrome</td>
<td>6 (5.3)</td>
<td>3 (2.7)</td>
</tr>
<tr>
<td>Hospital admissions for any post procedural clinically relevant complication</td>
<td>1 (0.9)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
# Eleview™ preliminary US market size assessment

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of colonoscopies in USA</td>
<td>16’000’000</td>
</tr>
<tr>
<td>Average number of adenomas found per colonoscopy in phase III trial</td>
<td>2,31</td>
</tr>
<tr>
<td>Use of injections on adenomas of difficult extraction requirements in phase III</td>
<td>8%</td>
</tr>
<tr>
<td>Number of vials used per adenoma</td>
<td>1,5</td>
</tr>
<tr>
<td>Foreseen price per vial</td>
<td>$ 81</td>
</tr>
</tbody>
</table>
Eleview™ market potential from additional indications

The tissues of the esophagus, stomach and duodenum are similar to those of the colon. Inspection of these conducted by Esophagogastroduodenoscopy (EGD).

Eleview™ can be used in all these tracts as many EGDs are performed as colonoscopies, both in the US and Europe. During EGD, removal of tissues/polyps is frequently necessary and will require Eleview™ as per below examples:

**Barretts Esophagus**
- Caused by GERD, ~1.6% of population affected
- Requires an EGD every 3 years
- Tissue removal required in ~10% all cases

**Stomach & duodenal polyps**
- Polyps requiring extraction are found in around 0.7% of all procedures
Development Status
- USA Approved
  Marketing trials in four sites ongoing
  (speed and safety versus standard care in EMR)
- EU Approved

Timing
- Launched in US May 2017

Business Development
- Licensing process in EU and RoW ongoing
Improve Lesion Detection
Colonoscopy: standard of care

What is the highest current standard of care in colonoscopies?

High Definition White Light Colonoscopy ("HDWL")
Requires sophisticated HD equipment and it is used in less than 20% of overall procedures

ISSUES

Even if using the best available tools, the Adenoma Detection Rate ("ADR") depends primarily on the subjective skill of the endoscopist
Quality Indicators for Colonoscopy and the Risk of Interval Cancer

Michał F. Kamiński, M.D., Jarosław Regula, M.D., Ewa Kraszewska, M.Sc., Marcin Polkowski, M.D., Urszula Wojciechowska, M.D., Joanna Didkowska, M.D., Maria Zwierko, M.D., Maciej Rupinski, M.D., Marek P. Nowacki, M.D., and Eugeniusz Butruk, M.D.

Risk of interval cancer by endoscopists with low ADR

Risk of interval cancer by endoscopists with high ADR

The more patients with adenoma are detected…
The more cancer is prevented
For each 1% increase in ADR:

**3% decline** in incidence of interval CRC

**5% decline** in incidence of fatal CRC
For every 5% improvement in ADR:

- **11% reduction** in CRC incidence
  (95%CI, 10.3-11.9)

- **13% reduction** in CRC death
  (95%CI, 11.1-13.7)

- **-3% cost due to saving in CRC treatment**

Every year in USA:

- 149,000 CRC cases
- 50,000 CRC deaths
- 14$ billion
According to the ASGE-ESGE, chromoendoscopy “is the topical application of stains or dyes at the time of endoscopy in an effort to enhance tissue characterization, differentiation, or diagnosis.”

**Chromoendoscopy is recommended in IBD patients to enhance detection of neoplasias**

However it is used in less than 10% of overall procedures.

**ISSUES**

dye needs to be prepared as a solution selectively sprayed and washed out before mucosa reading requires extensive cumbersome work and time relies too much on subjectivity of the operator
Improving the subjective skill of endoscopists in identifying dysplasia
Significantly enhances ADR substantially beyond HDWL and **FLAGS** lesions in a previously unseen, unrivalled fashion.
A one-of-a-kind trial

In ordinary trials, placebo is generally water and sugar

in our trial
Placebo is the highest standard of care (HDWL)

...performed

In some of the top hospitals by some of the top endoscopists in the world
A one-of-a-kind trial

**LuMeBlue** is not a medical device or a tool but a **fully fledged drug**. The LuMeBlue trial is the first multicenter and multinational trial in colonoscopy with extremely stringent requirements therefore raising the odds and hurdles but also the **overall reliability** of the result.
Significant edge against competitors

**PRIMARY ENDPOINT**
Proportion of subjects with at least one histologically proven Adenoma or Carcinoma

**MAIN SECONDARY ENDPOINT**
As of efficacy
- False positive rate
- Proportion of subjects with at least one histologically proven Adenoma

As of safety
- Adverse events
- Renal and Liver function tests
LuMeBlue significantly enhances ADR in the full analysis set FAS

<table>
<thead>
<tr>
<th></th>
<th>HDWL</th>
<th>LuMeBlue 200 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR</td>
<td>47.81%</td>
<td>56.29%</td>
</tr>
<tr>
<td>Relative risk increase*</td>
<td>17.7%</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td>0.0099</td>
</tr>
<tr>
<td>Odds Ratio</td>
<td></td>
<td>1.41 [1.09, 1.81]</td>
</tr>
</tbody>
</table>

*Calculated as (ADR_{LuMeBlue 200 mg} / ADR_{HDWL}) - 1
critical requirement: False Positive Rate (FPR) versus HDWL

Determining that LuMeBlue does not entice the endoscopist to remove lesions that are not proven to be adenomas (diagnostically, a False Positive).

The Agencies, forecasted a higher number of False Positive (FP) in the patients treated with LuMeBlue, allowing a FPR versus HDWL in the range of + (15% / 35%).

LuMeBlue instead showed a significantly lower FPR than HDWL, thus proving that with LuMeBlue the endoscopist:

**Finds more lesions** → **and more are proven to be adenomas**
LuMeBlue FPR is significantly better than HDWL

LuMeBlue decreases FPR by 14.4% vs HDWL

p-value: < 0.0001

Total LuMeBlue pts: 485
Total HDWL pts: 479
LuMeBlue is clinically superior to HDWL in the most important segment of patients

If adenomas are detected during colonoscopy, the subject will be referred to a next colonoscopy in a short time span ie 1-3 years

If no adenomas are detected during colonoscopy, the subject will be referred to a next colonoscopy in 10 years

- Missing an adenoma in this patient segment greatly increases the risk of an interval cancer
- Missed adenomas will generally be flat and small

75/80% of patients have few lesions and experience less than 3 excisions
**LuMeBlue efficacy has even greater diagnostic efficacy in largest market segment**

<table>
<thead>
<tr>
<th></th>
<th>ADR IN OVERALL PTS POPULATION</th>
<th>ADR IN PTS WITH EXCISION ≤ 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HDWL</td>
<td>HDWL</td>
</tr>
<tr>
<td></td>
<td>47.81</td>
<td>35.9</td>
</tr>
<tr>
<td>LuMeBlue</td>
<td>56.29</td>
<td>45.3</td>
</tr>
<tr>
<td>RRI</td>
<td>17.7%</td>
<td>26.2%</td>
</tr>
</tbody>
</table>

- **HDWL**
  - Pts 485
  - RRI 17.7
- **LuMeBlue**
  - Pts 479
  - RRI 26.2
LuMeBlue shows max diagnostic value increase in the segment with 0 - 1 excision

<table>
<thead>
<tr>
<th>ADR IN OVERALL PTS POPULATION</th>
<th>ADR IN PTS WITH EXCISION 0 - 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDWL</td>
<td>HDWL</td>
</tr>
<tr>
<td>LuMeBlue</td>
<td>LuMeBlue</td>
</tr>
<tr>
<td>RRI</td>
<td>RRI</td>
</tr>
<tr>
<td>HDWL</td>
<td>Pts 485</td>
</tr>
<tr>
<td>LuMeBlue</td>
<td>Pts 479</td>
</tr>
<tr>
<td>RRI</td>
<td>RRI 17.7</td>
</tr>
<tr>
<td>HDWL</td>
<td>Pts 233</td>
</tr>
<tr>
<td>LuMeBlue</td>
<td>Pts 264</td>
</tr>
<tr>
<td>RRI</td>
<td>RRI 38.2</td>
</tr>
</tbody>
</table>

| HDWL                         | Pts 485                      |
| LuMeBlue                     | Pts 479                      |
| RRI                          | RRI 17.7                     |
| HDWL                         | Pts 233                      |
| LuMeBlue                     | Pts 264                      |
| RRI                          | RRI 38.2                     |
LuMeBlue flags more diminutive adenomas than HDWL

<table>
<thead>
<tr>
<th></th>
<th>HDWL 200 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with diminutive adenomas</td>
<td>144</td>
</tr>
<tr>
<td>Percentage overall population</td>
<td>30.06%</td>
</tr>
<tr>
<td>Relative risk increase*</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td></td>
</tr>
<tr>
<td>Odds Ratio</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

Data from FAS
*Calculated as (ADRLuMeBlue 200 mg / ADRHDWL) - 1
LuMeBlue flags more subjects with non-polypoid lesions than HDWL

<table>
<thead>
<tr>
<th></th>
<th>HDWL</th>
<th>200 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts with non-polypoid lesions</td>
<td>168</td>
<td>213</td>
</tr>
<tr>
<td>Percentage overall population</td>
<td>35.07%</td>
<td>43.92%</td>
</tr>
<tr>
<td>Relative risk increase*</td>
<td></td>
<td>25.2%</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td>0.0056</td>
</tr>
<tr>
<td>Odds Ratio</td>
<td>1.45</td>
<td>[1.12, 1.88]</td>
</tr>
</tbody>
</table>

*Calculated as (ADRLuMeBlue 200 mg / ADRHDWL) - 1
LuMeBlue
US market research initial feedback

Number of colonoscopies in USA 16’000’000
Suggested price $175-200
Expected US market entry Q3 2018
Development status
  ● Phase III completed, primary endpoint “proportion of subjects with at least one histologically proven Adenoma or Carcinoma” attained

Timing
  ● NDA Filing targeted for H1 2017

Business Development
  ● Discussions for RoW licensing ongoing
Improve Efficiency

Remimazolam
Remimazolam: main features

- US cost bundling provides incentive to make procedures as fast as possible while reducing costs

- Procedural sedation is used in practically all colonoscopies in the USA
  - Market is split ~50%: 50% between propofol and midazolam

- Targeted to save costs
  - Propofol use require presence/availability of an anaesthetist in the US
  - As of 1.1.17 the cost of the anaesthetist needs to be bundled under the total procedure cost and is thus borne by the endoscopist
  - With an average reduction of 20 min/procedure vs Midazolam and an average number of procedures of 10-20/day/doctor, centers could increase throughput significantly when using Remimazolam

- One Phase III completed for colonoscopies and one underway for bronchoscopy

- Licensed in from PAION AG as an ideal marketing complement to LuMeBlue and Eleview™
Reduces Time to Reach Sedation

<table>
<thead>
<tr>
<th></th>
<th>Remimazolam</th>
<th>Placebo</th>
<th>Midazolam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start Procedure</td>
<td>4.0</td>
<td>19.5</td>
<td>19.0</td>
</tr>
<tr>
<td>MOAA/S 3</td>
<td>3.5</td>
<td>19.0</td>
<td>19.0</td>
</tr>
<tr>
<td>Peak Sedation</td>
<td>3.5</td>
<td>21.0</td>
<td>19.0</td>
</tr>
</tbody>
</table>
Reduces Time Back to Normal

End of procedure to fully alert

Time to back to normal (Patient Reported)

Remimazolam Placebo Midazolam

Remimazolam Placebo Midazolam

* R vs. M: Anova F-test for equal means in 2 groups
Cosmo’s pipeline covers unmeet needs in colonoscopies
Introducing...
● Cosmo Pharmaceuticals NV has recently incorporated fully owned Aries Pharmaceuticals Ltd, Dublin

● Aries Ltd is 100% holder of Aries Pharmaceuticals Inc., San Diego

● Aries Ltd will market in the US under a license and supply agreement LuMeBlue, Eleview™, Zemcolo and Remimazolam

● Aries Pharmaceuticals Inc. will act as a sales, marketing & distribution company on behalf of Aries Pharmaceuticals Ltd

● Aries sub-holding group is crafted to allow replication of “equity for product” strategy in respect of Cosmo Pharmaceuticals US pipeline

● Aries Inc. management team is incentivized with a fully-fledged ESOP scheme with Aries Ltd shares
ARIES management team

**TOM JOYCE**
President & Chief Executive Officer
From 2004 to 2014 Vice President, Marketing and National Accounts at Santarus. From 2014 to 2016 founder and partner of L.A.S. Partners, a health science consulting company focused on providing commercial insight and strategy to pharma and biotech companies. Has a B.A. in Psychology from the University of Dayton.

**BLAKE BOLAND**
Senior Vice President of Sales
From 2004 to 2014 Vice President of Sales at Santarus, where he developed and led a national sales team, from company start-up, through all growth stages and the company's ultimate $2.6 billion sale in 2014. Consultant of several biotech companies in commercial strategy, sales force structure, managed care, sales and management training. Has a B.A. in Business Administration from Graceland University and an M.B.A. from Rockhurst University.

**JON HEE**
Chief Commercial Officer
From 2004 to 2014 Vice President, Commercial Affairs at Santarus, where he commercialized products for the gastrointestinal disease, diabetes and other specialty markets. From 2014 to 2016 founder and partner at L.A.S. Partners (see above). Has an M.B.A. from Harvard University and a B.S. in Chemical Engineering from Stanford University.
Current ARIES set-up

- Leveraging on existing fruitful relationships, Cosmo has hired a US senior highly experienced management team located in San Diego
- Aries Inc. management team has a specific expertise in marketing and distribution of GI drugs and pharmaceuticals products
- Aries currently employs 45 Sales Reps, 7 Medical Science Liaison and 3 Regional Sales Managers
- Aries Inc. projected evolution of staff & salesforce according to preliminary marketing plans:

<table>
<thead>
<tr>
<th>Staffing Plan</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>95</td>
<td>247</td>
<td>316</td>
</tr>
<tr>
<td>Thereof hired sales persons</td>
<td>45</td>
<td>145</td>
<td>205</td>
</tr>
</tbody>
</table>

Staffing may vary depending on launch timings
Potential for Aries opportunistic IPO

- Cosmo will consider listing Aries Ltd in a yet-to-be-selected Stock Exchange when convenient
- Capture the future operational and financial value creation
Next Steps
We are working towards...

- File LuMeBue & Zemcolo NDA in USA
- Find Partners for LuMeBlue, Eleview™ & Zemcolo in RoW
- Further expand existing pipeline
Contacts

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