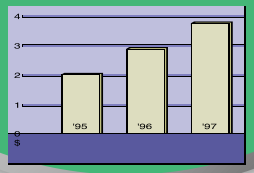
Transforming Strong Medicines into First-Line Therapies

ARSTAT Inc. – Combination Pill (Enhanta™)

A First-in-Class Therapy for Painful and Heavy Menstrual Periods

Novel, Predictably Efficacious and Safe Treatment for Concomitant Dysmenorrhea and Menorrhagia

Very Large, Undertreated Market; ≤4 Years to Launch; Could Capture Hundreds of Millions In Sales



- *Enhanta™ could be developed by either ARSTAT or a dedicated start-up.*
- *We may also pursue early out-licensing opportunities.*
- *The R&D costs and milestones, funding and exit details are disclosed below.*

Contact: Arkady Rubin, PhD. E-mail: arubin@arstatinc.com Tel: 347-385-0878

Introduction

- *The company has developed and patented Enhanta™ (a novel oral drug formulation) for the treatment of painful and heavy menstrual periods*
- *This condition (diagnosed as concomitant dysmenorrhea and menorrhagia) is highly prevalent; however, it currently lacks a single, specific non-hormonal therapy. Enhanta™ addresses this significant unmet medical need.*
- *Based on the wealth of available data, we designed a pill combining an NSAID (first-line for menstrual pain) and a small fraction of an approved dose of tranexamic acid (first-line for excessive menstrual bleeding).*
- *With predictable safety and efficacy, a probability of successful development is very high. Enhanta™ could capture hundreds of millions in sales.*
- *The patent applications are developed by the ARSTAT's principal - Arkady Rubin, PhD., a researcher with 20+ years of pharma industry experience, mostly in women's health.*
- *Dr. Rubin is expertly knowledgeable in the treatment of dysfunctional uterine bleeding; he has analyzed extensive clinical databases and co-authored related publications. He was also a co-inventor of Ortho Tri-Cyclen Lo®, the best-selling oral contraceptive in the US (>$450M in 2013).*
- *To advance Enhanta™, the principal seeks partner(s) experienced in pharmaceutical start-ups. The last three slides present related details.*

Novel, Proprietary Oral Combination (NSAID + Low Dose Tranexamic Acid) *for Painful and Heavy Menstrual Periods*

Enhanta™: Clinical and Commercial Highlights

- ***New medical use of well known drugs with established efficacy and safety***
- ***A low-cost, low-risk development of two valuable formulations (Rx and OTC)***
- ***Clinical testing begins with Phase IIb or Phase III; a 505(b)(2) NDA pathway***
- ***Unlike NSAID alone (first-line therapy), the combination adequately reduces menstrual bleeding and keeps NSAID at minimal dose effective for pain***
- ***Robust clinical data strongly supports superiority of the combination vs. NSAID in the reduction of bleeding (a primary efficacy endpoint in Phase III)***
- ***≈4 years and ≈$17M to the US market (<$20M to both US and EU markets)***
- ***A substantially improved first-line therapy in a large, undertreated market***
- ***Hundreds of millions in potential annual sales for both Rx and OTC***
- ***Great exit opportunities for VC (earliest exit in ≤2 yeas, after Phase IIb study)***

Strong Proprietary Position

- ***Our innovation:*** *An oral combination of NSAID & low-dose antifibrinolytic (tranexamic acid) was never considered before. Clinical data supports this formulation as a preferred therapy for painful and heavy menstrual periods.*
- ***Three patent applications:*** *(US provisional, non-provisional (PCT), and German utility model), developed with a top IP firm (Fish & Richardson)*
  - Applications support multiple candidates with various NSAIDs (ibuprofen, naproxen, etc.) and different doses of tranexamic acid.
  - The PCT application is currently pursued in the US.
  - A 10-year protection of all compositions is already secured in Germany.
- ***Novel, proprietary*** *oral drug formulations with no similar predecessors*
- ***Novel:*** *a tranexamic acid dose is dictated by the NSAID's ability to reduce menstrual bleeding and by clinical targets in the treatment of menorrhagia*
- ***Novel:*** *both amounts of tranexamic acid in the oral formulations and total daily doses are much lower than those currently marketed or ever tested*
- ***Novel:*** *daily dosing regimens for target populations (e.g., women diagnosed with dysmenorrhea/menorrhagia or without clinical diagnoses)*

Painful and Heavy Menstrual Periods - Prevalent and Undertreated

❖***Highly Prevalent:***

- ***5.6 Million (US) with dysmenorrhea (painful menstrual periods)***
- ***22 Million (US) with menorrhagia (heavy menstrual bleeding)***
- ***20 Million (US) with uterine fibroids may have both***
- ***Days of painful and heavy menstrual periods may be experienced by most women not clinically diagnosed with dysmenorrhea and/or menorrhagia***

❖***Current Treatments Not Optimal:***

- ***Combined contraceptives (off-label) – hormonal side effects, loss of fertility***
- ***Progestin-only contraceptives – same as above + permanent amenorrhea***
- ***Androgens – rarely administered due to serious tolerability issues***
- ***Endometrial ablation – inferior efficacy, temporary amenorrheic state***
- ***Hysterectomy (severe cases) – permanent infertility, morbidity, high cost***

❖***Underdiagnosed and Undertreated Market:***

- ***Lack of disease awareness***
- ***Poor safety and efficacy of existing therapies***

NSAIDs (Current First-Line) - Great for Pain, Inadequate for Bleeding

- ***Can't Do with NSAID alone:***

- *NSAIDs - first-line ("off-label") therapy for painful & heavy menstrual periods*
- *Women with painful menstrual cramps (dysmenorrhea) have high levels of prostaglandins. NSAIDs act by blocking prostaglandin production.*
- *NSAIDs' efficacy in menstrual pain is well established.*
- *Some NSAIDs are indicated for primary dysmenorrhea (menstrual cramps in the absence of any underlying abnormality) and available by prescription*
- *At relatively low doses, the NSAIDs can be purchased over-the-counter*
- *The NSAIDs also reduce menstrual blood loss by binding to prostaglandin receptors which are significantly increased in women with menorrhagia*
- *In a majority of women, reduction of menstrual bleeding is not inadequate at doses approved for pain. Maximal NSAID doses must often be administered.*
- *Higher NSAID doses increase the risk of GI, CV and other side effects.*

Antifibrinolytic – Good for Bleeding, At High Doses - Unsafe with NSAIDs

- ***Can't Add Antifibrinolytic (Tranexamic Acid) at Approved Dose:***

  - *Tranexamic acid, TA (Lysteda®) - first-line therapy for menorrhagia.*
  - *For better bleeding control, co-administration of NSAID and TA was considered.*
  - *At approved TA dose, concurrent therapy may be unsafe (not recommended)*
  - *Approved Lysteda daily dosing regimen (US): two 650-mg tablets (1,300mg) x 3, i.e., 6 tablets = 3,900 mg/day*
  - *Typical European regimen: two 500-mg tablets (1,000mg) x 4 = 4,000 mg/day*

- ***Low-dose tranexamic acid oral formulations are not available***

  - *Utility of tranexamic acid at the approved and/or available doses restricted to women who have menorrhagia without dysmenorrhea.*
  - *For an efficacious and safe use of tranexamic acid in women with both conditions, NSAID's ability to reduce bleeding should not be ignored.*

Enhanta™: Ideal Solution with Strong Supporting Data

The Candidate	• Keeps NSAID at minimal effective dose for pain • Adds low dose tranexamic acid (15-25% of approved Lysteda® dose) for much better bleeding control • Predictably safe at recommended doses
Robust Clinical Data	• Antifibrinolytic (tranexamic acid) – well established dose-response for both efficacy and safety • NSAID component - known reduction of menstrual bleeding • Predictable overall reduction of menstrual blood loss
Additive mechanisms	• Dictate doses for each component • Allow optimal doses for various levels of menstrual pain and menstrual bleeding (Rx, OTC) • Ensure superior efficacy of a combination vs. NSAID alone

Clinical Rationale – Additional Details

NSAID approved for menstrual pain: Reduces menstrual bleeding by ≈30% (historical data)

→ ***In a majority of women, amount of menstrual blood loss still exceeds normal or acceptable levels***

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Antifibrinolytic (tranexamic acid) supplement: at a fraction of approved dose reduces menstrual bleeding by ≈10%-15% (historical data)

→ ***<u>Important</u>: Incremental reduction of menstrual bleeding significantly improves women's satisfaction and quality of life metrics (strong supporting data)***

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Enhanta™: At least 40% reduction of menstrual blood loss

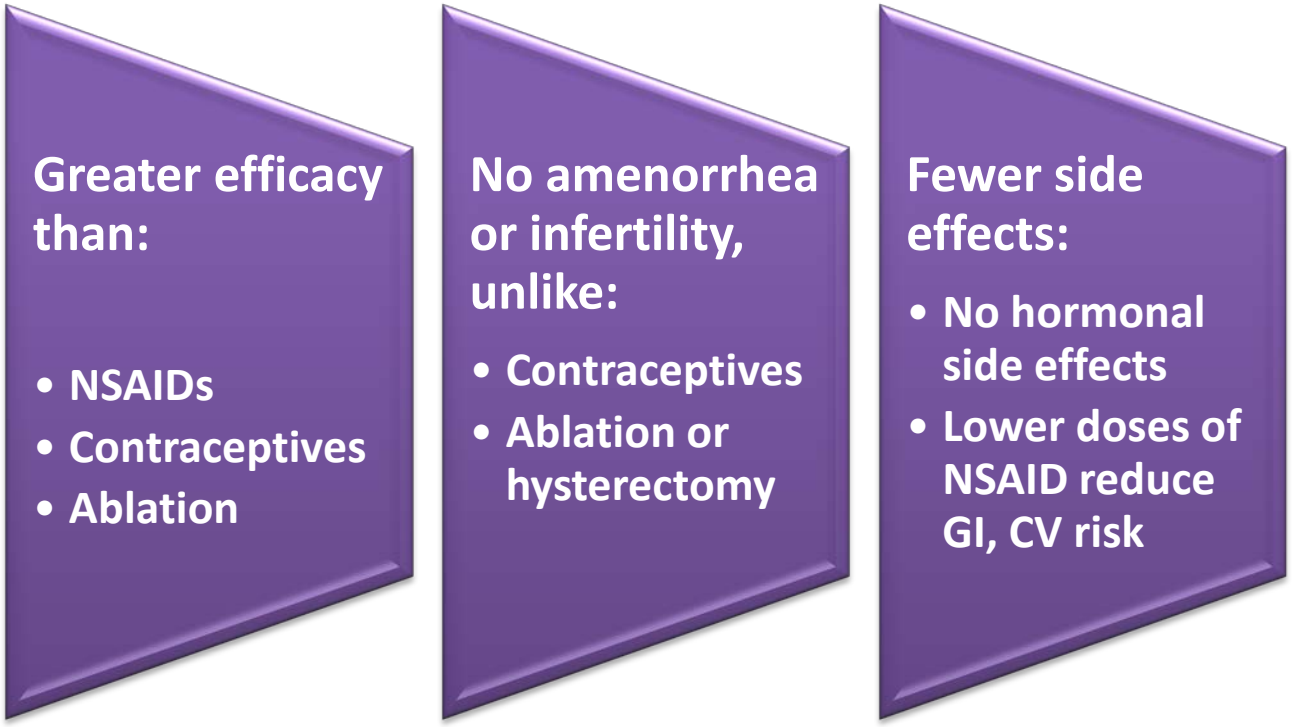
→ ***Meets US & European clinical and regulatory targets for treatment of heavy menstrual bleeding***

Development Details

- *Data supports successful development of both Rx & OTC versions:*
  - Rx - for women diagnosed with dysmenorrhea and/or menorrhagia;
  -OTC - for women perceiving their menstrual periods as heavy & painful
- *Clinical testing begins with Phase IIb. An aggressive option – start with Phase III (two drug combinations will be tested in the 1st Phase III study)*
- *Individual components are approved; 505(b)(2) NDA can be utilized*
- *Recommended NSAID and doses of tranexamic acid will be disclosed*
- *Known regulatory precedents and approvability criteria*
- *Per regulations for combination drugs, a formal proof of analgesic efficacy (the candidate's ability to relieve menstrual pain) not required*
- *Clinical data also strongly supports superiority of the combination pill vs. NSAID alone in the reduction of menstrual bleeding (a primary efficacy endpoint in a future Phase III study)*
- *≈4 years & <$17M to US Market (<$20M to both US and EU Markets)*
- *Active agents of the combination drug formulation are out of patent and may be purchased from multiple suppliers.*

Clinically and Commercially Appealing

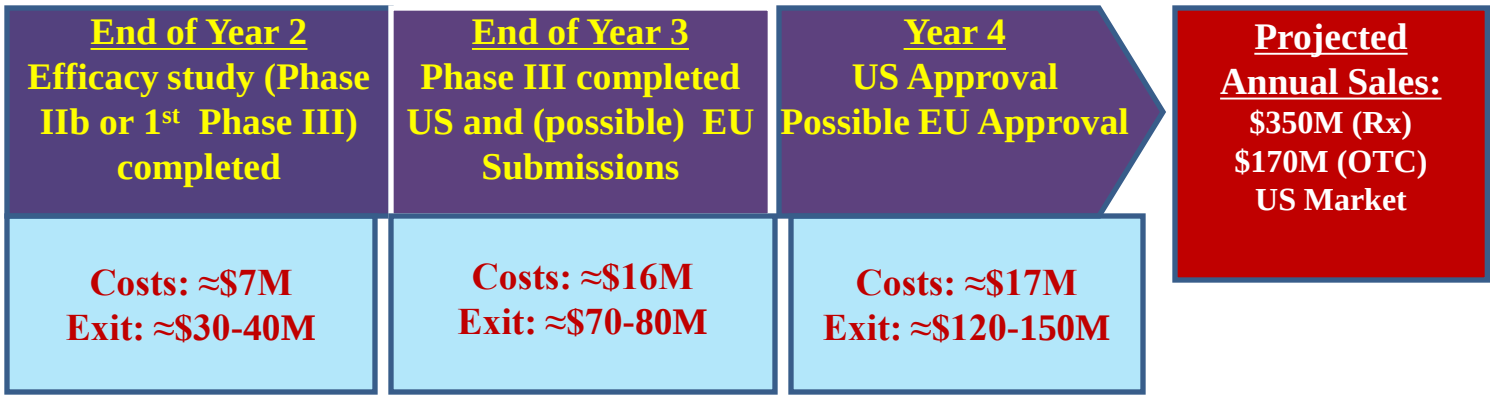
❖ Superior Efficacy and Safety – Potential First-Line



❖ Could Capture Significant Sales

- *Rx version: 20%-25% of the market ($≈350M/year)*
- *OTC version may capture another 10% (≈$170M/year)*
- *These are US estimates; global sales must be substantially higher.*

R&D Costs, Major Milestones and Exit Opportunities: Overview



***Costs** = **Cumulative** R&D costs (i.e., $17M at Year 4 are the **total R&D costs**);*
***Exit** = **Upfront payments** to all shareholders (royalties are also expected)*

Notes: (1) The cost estimates are for the US only. Extra funding (≈$3M) may be needed for the EU submission.
(2) For exit opportunities, a US-only scenario is presented. With EU approval, exits are expected to be greater.
(3) All development metrics are for the Rx version. For OTC, modest extra funding will be needed years 3-4.
The OTC version (available both in the US and in EU) will increase the value of this proposal.

Business Model

- ***Our business plan is to advance Enhanta™ up to completion of the first efficacy study (Phase IIb or Phase III) and to commercialize it in 2.5 years or less.***
- ***Enhanta™ could be developed by either ARSTAT or a new start-up with well-defined development targets and great exit opportunities.***
- ***We will pursue a strategic R&D partnership or a licensing agreement.***

Seeking Business Partner

- ***The principal seeks one or two co-founders for the specialty start-up dedicated to development of this candidate***
- ***Ideally, it will be an angel investor experienced in pharmaceutical start-ups. Please take a look at the last slide for details***
- ***It could also be an industry veteran in search of a new venture.***
- ***The co-founder's expertise in women's health and/or connections to VC entities would be an asset***
- ***If interested, the partner may assume an executive position (possibly, CEO) within the new company***

Business Plan Details

- ❖ *Over the next 12 months, the following milestones will be achieved:*
- ❖ *A meeting with the FDA will confirm the clinical program and a 505(b)(2) NDA path (based on US precedents, we expect to run 2-3 relatively small efficacy studies and one PK trial).*
- ✓ *Following the meeting, an Investigational New Drug application (IND) will be filed.*
- ✓ *Meetings with Health Authorities to confirm the filing requirements for major EU markets (based on initial input from European regulatory experts, we do not plan ex-US studies).*
- ✓ *Ready to start the first clinical study (Phase IIb or Phase III) in the US*
- ✓ *Continued prosecution of the patent application; the US patent could be issued.*
- ❖ *Accomplishment of these tasks is expected to secure a licensing agreement or a Series B round of financing which would be applied toward the completion of the 1st clinical efficacy study.*

The Value Proposition

- ***To support Enhanta's research and business development activities, the company seeks to raise $400-500K from angel investor(s) in exchange for the company's equity***
- ***A year from now, Enhanta's valuation is expected to increase at least 5-6-fold, bringing it to $10-12M.***
- ***In 2.5 years, we will offer the investors an opportunity for exit or to continue with their support. The anticipated return could be 10-12x.***