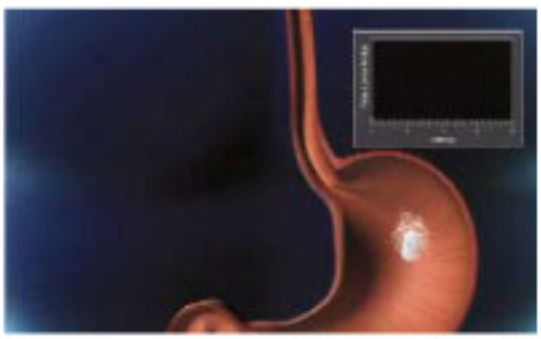
MiddleBrook PHARMACEUTICALS™

How PULSYS™ Products Work

1

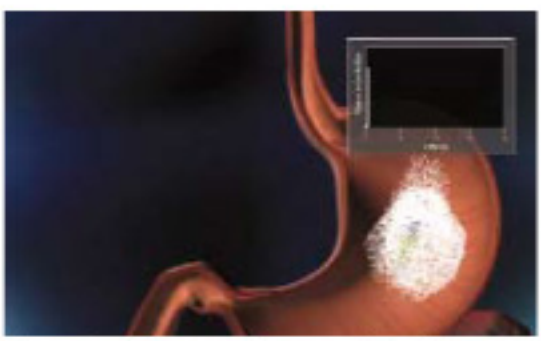
A PULSYS™ product is ingested as a film-coated tablet, like any other medication a patient might swallow.

2



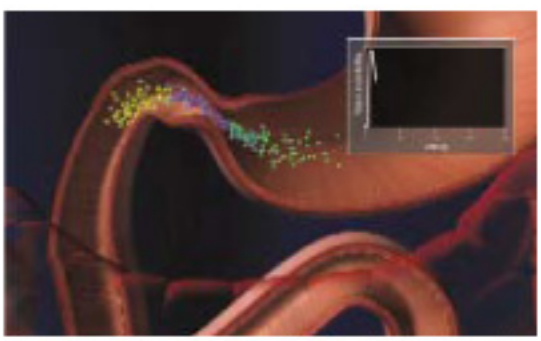
PULSYS™ tablets are specifically designed to release the drug in rapid, staccato bursts—or pulses—at specific regions within the GI tract.

3



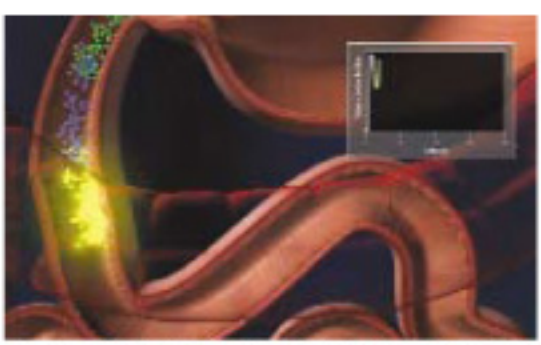
Once the tablet enters the stomach, it disintegrates and releases the first pulse, or dose, of drug.

4



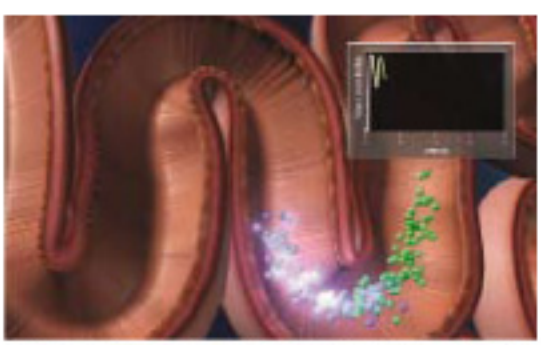
Up to six different types of pellets (pulses) are formulated to release at various points throughout the GI tract.

5



A second pulse may release immediately in the pylorus, after entering the small intestine.

6

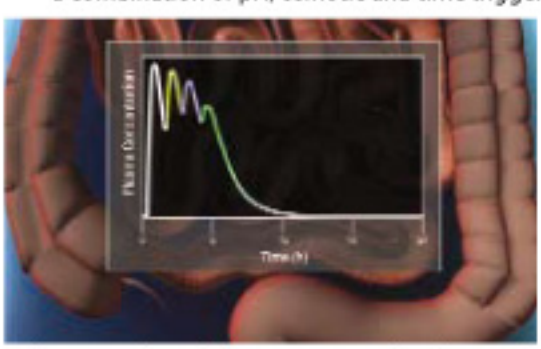


The additional pulses continue to move throughout the GI tract and release more drug dose in a controlled and programmed manner, using a combination of pH, osmotic and time triggers.

7

Since the pellets travel along the lumen wall of the small intestine, they have a more consistent GI transit compared to other solid dosage forms, such as sustained release tablets.

8



The pulses are released in a programmed and reproducible profile. The PULSYS™ product is fully delivered within the first few hours of the once-daily dose.

MiddleBrook PHARMACEUTICALS™

PULSYS™ Products

Redefining Infectious Disease Therapy

MiddleBrook is a pharmaceutical company focused on developing and commercializing pulsatile drug products that fulfill unmet medical needs in the treatment of infectious disease. MiddleBrook is developing a broad portfolio of drugs based on the novel biological finding that bacteria exposed to antibiotics in front-loaded, sequential bursts, or pulses, are killed more efficiently and effectively than those exposed to standard antibiotic treatment regimens. Based on this finding, MiddleBrook has developed a proprietary, once-a-day pulsatile delivery technology for antibiotics and other anti-infectives called PULSYS™. By examining the resistance patterns of bacteria and applying its improved technologies, MiddleBrook has the potential to redefine bacterial infection treatment and significantly improve drug efficacy, shorten length of therapy, and reduce the emergence of antibiotic resistance versus currently available antibacterial products.

PULSYS™ Technology Platform

Based on its novel biological finding that rapid sequential pulsatile dosing of antibiotics may offer therapeutic advantages, MiddleBrook has developed the PULSYS™ oral drug delivery system and MAPS™, an enabling technology for the design of the PULSYS™ products. MAPS™ is a proprietary analysis and design system that utilizes the physical, chemical, biological and microbiological properties of each specific antibiotic to design the optimum PULSYS™ product. The PULSYS™ dosage form is a compressed tablet that contains pellets designed to release drug at different regions in the gastrointestinal tract in a pulsatile manner. The dosage form is made up of multiple pellet types of varying release profiles that are combined in a proportion so as to produce a constant escalation in plasma drug levels in the early portion of the dosing interval. The transit properties of pellets enhance the overall absorption-time window and offer improved bioavailability compared to tablet matrix forms. In all cases, the MiddleBrook PULSYS™ products will be once-a-day products. The PULSYS™ system utilizes well-studied excipients and common manufacturing processes. The development of the PULSYS™ delivery system is well advanced and clinical pharmacokinetic studies have been completed on several currently marketed antibiotics with varying therapeutic and physico-chemical profiles. MiddleBrook has a strong intellectual property position on the therapeutic benefits of pulsatile dosing and the associated drug delivery technologies. Sixteen of these patents are issued and allowed to date. In addition to antibiotics, MiddleBrook believes that this approach may find utility in antiviral and antifungal therapies to expand its anti-infectives franchise. Applications in oncology could further expand MiddleBrook' focus over the mid- to long-term. The MiddleBrook patent estate covers all of these opportunities.

The PULSYS™ Advantage

MiddleBrook™ products under development may provide patients with more convenient alternatives to current antibiotics, making treatment regimens easier to follow. Each is designed to be taken orally, once daily. But the benefits may go much further. For some antibiotics and infections, the duration of therapy could be significantly reduced. For others, a lower daily dose may be achievable. MiddleBrook plans to market all products as once daily treatments with most dosing regimens targeted for three to five days. This is in significant contrast to currently available drugs, which are taken two, three, or four times a day for as long as 14 days. There may be one or more products consisting of a single dose for the entire treatment of a particular infection. Studies in human subjects show that the PULSYS™ system performs well in terms of strong pulses, as demonstrated by appropriate blood levels.

The PULSYS™ Advantage

- Improved efficacy or killing efficiency
- Reduced bacterial resistance
- Once-daily dosing
- Shorter overall duration of therapy
- Lower daily dose
- Improved side effects profile