DURECT

SABER™
Depot Injection Technology

The SABER Delivery System is an injectable, biodegradable delivery system that uses a high viscosity carrier such as sucrose acetate isobutyrate (SAIB) and one or more pharmaceutically acceptable additives. The drug to be delivered by the SABER Delivery System is dissolved or dispersed in a SABER system for subsequent injection. Upon injection, the SABER system forms a depot from which the drug is delivered at a controlled rate over periods of a few days to 3 months or more. Both water soluble and insoluble drugs of small and large molecules can be formulated, sterilized and released from SABER depot injection systems.

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SABER™ Depot Injection Technology

SABER Depot Injection Technology has the following potential advantages:

Control of Initial Delivery Rates. The SABER depot can provide improved control of initial release rates, resulting in significantly lower burst of drug than is typical of polymer-based systems. *In vivo* delivery of a small therapeutic molecule from a clinical SABER formulation produced a flat pharmacokinetic profile with very little burst. *In vivo* delivery of a therapeutic protein from a SABER formulation was compared with that from a commercially available PLGA microsphere formulation. Ten-fold lower burst was observed with the SABER formulation.

High Drug Payload. Higher doses and smaller injection volumes than typical polymer based formulations.

Peptide/ Protein Delivery. SABER formulations isolate peptides and proteins in a non-aqueous non-polymeric solution to prevent premature exposure to water, which can lead to better drug stability and help minimize burst while modulating release over long periods of time.

Ease of Administration. Small needle gauges, small injection volumes and low solution viscosity result in easier, less painful administration.

Ease of Manufacture. Compared to microspheres and other polymer-based systems, SABER is readily manufacturable at low cost using standard equipment and processes for small volume parenteral injections.

Strong Patent Protection. DURECT has a strong intellectual property position covering SABER, SABER-like materials, and various applications of this technology to pharmaceuticals, biotechnology and drug delivery.

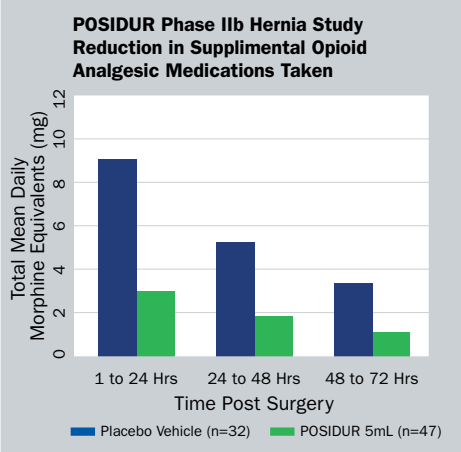
SABER Depot technologies can deliver drugs most effectively for one week to one month, with minimal injection site impact.

Examples of SABER in use - POSIDUR™

Our post-operative pain relief depot, POSIDUR, is a sustained-release injectable using our SABER system to deliver bupivacaine, an off-patent anesthetic agent. POSIDUR is designed to be administered to a surgical site at the time of surgery for post-operative pain relief and is intended to provide local analgesia for up to 3 days, which we believe coincides with the time period of the greatest need for post surgical pain control in most patients.

In July 2007, DURECT announced positive results from a 122 patient Phase IIb clinical trial of POSIDUR for the treatment of post-operative pain in patients undergoing inguinal hernia repair. In the trial, POSIDUR demonstrated statistically significant reductions in pain (approximately 30%) and total consumption of supplemental opioid analgesic medications (approximately 3-fold) versus placebo (see Figure 1).

FIGURE 1.



Posidur is in Phase III clinical trials in the U.S., and Phase II in Europe.

Examples of SABER in use – Proteins and Peptides

DURECT has conducted successful preclinical programs using SABER Depot System for the delivery of small molecular weight drugs, human growth hormone, interferons and various classes of proteins and peptides. These studies have shown the feasibility of producing longer term delivery of proteins and peptides of varying duration up to one month. To support our programs delivering proteins and peptides, DURECT has put in place various process equipment systems that include both freeze drying and spray drying of these active ingredients (see Figure 2).

FIGURE 2.

We are capable of filling of powders, viscous liquids and gels in vials and syringes. In addition, we are capable of manufacturing and packaging preclinical and clinical supplies in compliance with all FDA and international regulatory requirements.

In collaboration with various pharmaceutical and biotechnology partners, DURECT is developing innovative controlled-release drug products based on the SABER delivery system.

Table 1 shows a list of actual accomplishments as to how SABER Depot technology helps our partners create opportunities in new depot products.

TABLE 1.

Advantages of SABER™ Depot Systems

- Reduces the frequency of dosing, thereby lowering the cost of care and improving quality of life to patients.
  1. Reducing 9-18 IV infusion treatments of anti-cancer agents to 1 SC injection
  2. Reducing daily SC injection of peptides or proteins to once weekly SC injection
  3. Reducing weekly SC or IM injection of proteins/peptides to once monthly SC injection
- Reduces the C_{max}/C_{min} ratio, thereby potentially improving drug efficacy and decreasing the toxicity or side-effects
- Extends product life cycles