

DURECT CORPORATION

SABER™ Depot Injection Technology



Overview

The SABER Delivery System is an injectable, biodegradable delivery system technology 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 System is dissolved or dispersed in a SABER formulation 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.

DURECT welcomes your inquiries on product feasibility or development opportunities for your drug products that could benefit from our advanced drug delivery technologies.

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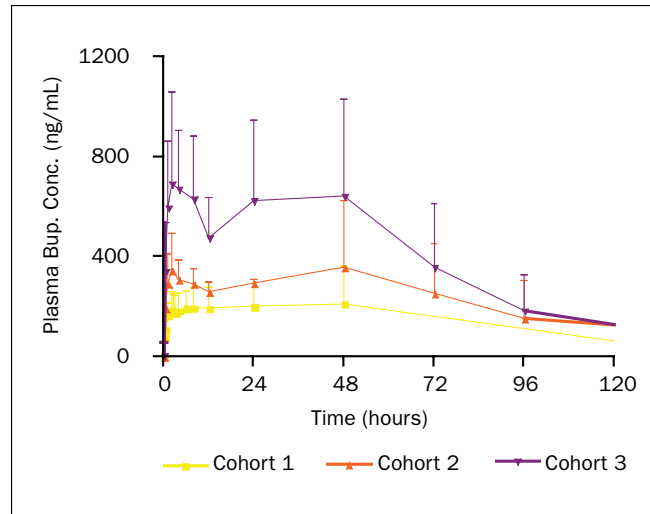


Figure 1
Mean plasma bupivacaine levels after administration of three different doses of bupivacaine (AUC is proportional to dose).

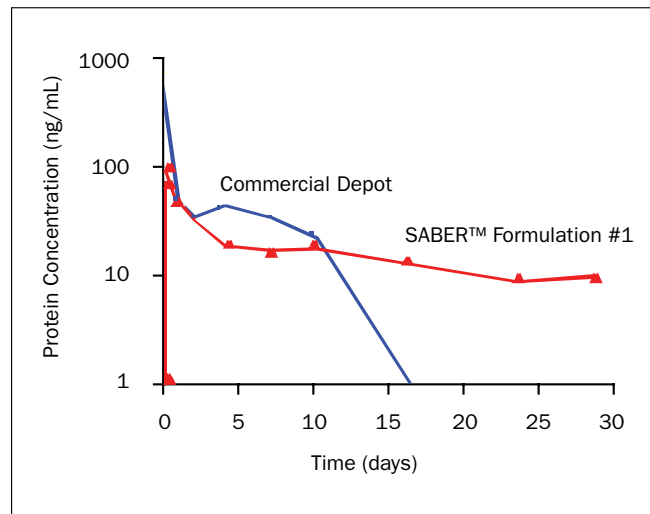


Figure 2
Preclinical evaluation illustrates sustained delivery profile of a recombinant protein from the SABER delivery system compared to a microsphere formulation of the same protein (note low protein burst observed with SABER delivery system).

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 molecule therapeutic from a clinical SABER formulation produced a flat pharmacokinetic profile with very little burst (See Figure 1). 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 (See Figure 2).

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.

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. This Phase IIb trial was designed to be the study upon which DURECT and its collaborator Nycomed would base their decision for advancing POSIDUR into Phase III clinical trials. In the trial, POSIDUR demonstrated statistically significant reductions in pain and total consumption of supplemental opioid analgesic medications versus placebo. These results are summarized in the two tables shown below and triggered an \$8 million milestone payment by Nycomed to DURECT under the parties' collaborative agreement.

Examples of SABER in use – Proteins and Peptides

DURECT has conducted successful preclinical programs using SABER Depot System for the delivery of sustained release forms of 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, with administration via small gauge needles. To support our programs delivering proteins and peptides, we have put in place aseptic processing of proteins and peptides including spray drying and freeze drying. We are capable of aseptic filling of powders, viscous liquids and gels in vials and syringes. In addition, we are qualified to manufacture 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.

POSIDUR™ Clinical Data

	Pain Control			
	Placebo	POSIDUR™ 5mL	% Change	p-value
Mean Pain Intensity on Movement AUC (a)				
1-72 hours	3.60	2.47	-31%	0.0033 (b)
1-48 hours	3.86	2.52	-35%	0.0007 (b)

(a) Normalized AUC based on numerical ratings scale for pain intensity of 0-10, with 0 being no pain.
(b) Using ANCOVA model.

	Consumption of Supplemental Opioid Analgesic Medication				
	Placebo	POSIDUR™ 5mL	% Change	Ratio (a)	p-value
Proportion of patients Taking Supplemental Opioid Analgesic Medication	72%	53%	-26%	-	0.0909 (b)
Supplemental Opioid Analgesic Medication Taken (c)					
1-24 hours	9.24	2.64	-71%	3.5	0.0009 (d)
24-48 hours	4.97	1.70	-66%	2.9	0.0190 (d)
48-72 hours	3.20	0.90	-72%	3.6	0.0172 (d)
Median Time to First Use of Supplemental Opioid Analgesic Medication (hours post-surgery)	2.7	>72.0	-	-	0.0197 (e)

(a) Fold difference between Placebo and POSIDUR™ 5mL
(b) Using Cochran-Mantel-Haenszel test.
(c) Total mean daily consumption in morphine equivalents
(d) Using ANCOVA model
(e) Using Log-Rank test for comparison of Kaplan-Meier survival cures

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