DURECT Reports Positive Results from POSIDUR(TM) Phase IIb Hernia Trial, Triggering $8 million Milestone Payment from Nycomed

Phase IIb Trial Achieves Statistically Significant Reductions in Pain and Total Consumption of Supplemental Opioid Analgesic Medications Versus Placebo

CUPERTINO, Calif., July 17 /PRNewswire-FirstCall/ — DURECT Corporation (Nasdaq: DRRX) announced today positive results from a 122 patient Phase IIb clinical trial of POSIDUR(TM) for 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 successful results trigger an $8 million milestone payment to be made by Nycomed to DURECT under the parties' collaborative agreement. In preparation for the Phase III program, DURECT has scheduled an end-of-Phase II meeting with the U.S. Food and Drug Administration (FDA).

(LOGO: http://www.newscom.com/cgi-bin/prnh/20020717/DRRXLOGO)

"We believe that the results of our Phase IIb trial support the validity of our POSIDUR product concept of simultaneously relieving pain while reducing opioid consumption," stated James Brown, President and CEO of DURECT Corporation. "Our partnership with Nycomed provides us with financial and development support along with a strong marketing presence to commercialize POSIDUR in Europe and other countries. We intend to market POSIDUR ourselves in the U.S., if approved, thus providing us with a pathway to establishing our own specialty pharmaceutical business."

Phase IIb Inguinal Hernia Trial

Design

The POSIDUR Phase IIb clinical trial was designed to evaluate the tolerability, activity, dose response and pharmacokinetics of POSIDUR in patients undergoing open inguinal hernia repair. The study was conducted in Australia and New Zealand as a multi-center, randomized, double blind, placebo-controlled study in 122 patients. Study patients were randomized into three treatment groups: patients that were treated with POSIDUR 2.5 mL (n=43), POSIDUR 5 mL (n=47) and placebo (n=32). The co-primary efficacy endpoints for the study were Mean Pain Intensity on Movement area under the curve (AUC), a measure of pain over a period of time, 1-72 hours post-surgery, and the proportion of patients requiring supplemental opioid analgesic medication during the study. Secondary efficacy endpoints included Mean Pain Intensity on Movement AUC over the period 1-48 hours post-surgery, mean total consumption of supplemental opioid analgesic medication, and time to first use of supplemental opioid analgesic medication. The threshold for statistical significance was considered to be at the $p<0.05$ level.

Results

Pain Control

In relation to the co-primary endpoint of pain reduction as measured by Mean Pain Intensity on Movement AUC 1-72 hours post-surgery, the patient group treated with POSIDUR 5 mL reported thirty-one percent (31%) less pain versus placebo (p=0.0033). A thirty-five percent (35%) reduction of pain as measured by Mean Pain Intensity on Movement AUC for the period 1-48 hours post-surgery, a secondary endpoint measure, was reported between the POSIDUR 5 mL treatment group versus placebo (p=0.0007).

	Placebo	Pain Control POSIDUR(TM) 5 mL	% 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 a numerical ratings scale for pain intensity of 0-10, with 0 being no pain.

(b) Using ANCOVA model.

Consumption of Supplemental Opioid Analgesic Medication

Fifty-three percent (53%) of the study patients in the POSIDUR 5 mL group took supplemental opioid analgesic medications versus seventy-two percent (72%) of the placebo patients (p=0.0909). Although this positive trend for this co-primary endpoint in favor of the POSIDUR 5 mL group was not statistically significant, both secondary endpoints measuring opioid analgesic medication consumption were met at a statistically significant level. During

the periods of 1-24 hours, 24-48 hours and 48-72 hours after surgery, placebo patients consumed approximately 3.5 (p=0.0009), 2.9 (p=0.0190) and 3.6 (p=0.0172) times more supplemental opioid analgesic medications (mean total daily consumption of opioid analgesic medication in morphine equivalents), respectively, than the POSIDUR 5 mL treatment group. In addition, the median time to first use of supplemental opioid analgesic medication after surgery for the placebo patients was 2.7 hours versus >72 hours for the POSIDUR 5 mL treatment group (p=0.0197).

Consumption of Supplemental Opioid Analgesic Medication

	Placebo	POSIDUR(TM) 5 mL	% Change	Ratio (a)	p-value
Proportion of Patients Taking Supplemental Opioid Analgesic Medications	72%	53%	-26%	-	0.0909 (b)
Supplemental Opioid Analgesic Medications 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(TM) 5 mL.
(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 curves.

Dose Finding

POSIDUR administered at the dose of 5 mL showed statistically significant activity relative to placebo whereas POSIDUR administered at 2.5 mL showed a positive trend relative to placebo on certain parameters but the results were not statistically significant. DURECT intends to select POSIDUR 5 mL as the dose to use in the Phase III program.

Safety

The patient groups treated with POSIDUR 5 mL and POSIDUR 2.5 mL showed comparable safety profiles as the patient groups treated with placebo, and the drug administration appeared well tolerated. The side effects commonly observed with opioid medication use were less frequent in the POSIDUR 5 mL and 2.5 mL treatment groups compared to placebo.

Other Exploratory Phase II studies

In addition to the Phase IIb study described above, DURECT has also been conducting smaller exploratory Phase II studies in hernia, shoulder arthroscopy and appendectomy surgeries to evaluate different application techniques, clinical design and conduct as well as other investigational factors. These trials have been conducted in multiple cohorts, generally consisting of approximately 6-21 patients in each treatment group. Hernia and shoulder studies have been completed while an appendectomy study is on-going. In all the exploratory studies, patient groups treated with POSIDUR 5 mL and POSIDUR 2.5 mL showed comparable safety profiles as the patient groups treated with placebo, and the drug administration appeared well tolerated. Some treatment groups from the hernia and shoulder exploratory studies utilizing POSIDUR have shown positive activity as measured by reduction of pain or consumption of supplemental opioid analgesic medication versus placebo, while other treatment groups have not. We are continuing to evaluate these studies to understand the different results observed, and intend to apply our learnings in the design of our Phase III program.

Conference Call Information

DURECT Corporation will be hosting a conference call to discuss this announcement on July 17, 2007 at 11:00 AM Eastern Time / 8:00 AM Pacific Time. To participate in the conference call, please dial in to (800) 254-0499 (domestic) or (408) 960-7131 (international) and request the “DURECT Corporate Event,” entry code 5020. Please dial in 10 minutes prior to the scheduled start time. An audio rebroadcast will be available one hour after the conference ends for 24 hours. The replay dial-in number within the US is 1-800-642-1687 (Reservation #: 7221981). The international replay dial-in number is 1-706-645-9291. The conference call is also available live over the Internet at http://www.www.durect.com.

About POSIDUR

POSIDUR is a long-acting local anesthetic under development by DURECT and Nycomed for the treatment of post-surgical pain. It is intended to be administered during surgery, where it continuously releases therapeutic levels of bupivacaine in a controlled fashion, providing up to 72 hours of uninterrupted local analgesia. POSIDUR’s performance is due to DURECT’s patented SABER(TM) delivery system, an injectable, biodegradable drug delivery technology.

About the DURECT / NYCOMED Collaboration

In November 2006, DURECT signed a collaboration agreement with Nycomed, a privately-held European pharmaceutical company headquartered in Switzerland, whereby the companies are jointly developing DURECT’s POSIDUR post-operative pain relief depot. Under the terms of the agreement, Nycomed paid DURECT an upfront license fee of $14 million; with the payment of the $8 million clinical development milestone described above, DURECT may earn additional

milestone payments of up to $180 million due upon achievement of additional defined development, regulatory and sales milestones. The two parties are jointly directing and equally funding a development program for POSIDUR intended to secure regulatory approval in both the U.S. and the European Union (E.U.). DURECT has licensed Nycomed the exclusive commercialization rights to POSIDUR in the E.U. and select other countries. In addition, DURECT will manufacture and supply the product to Nycomed for commercial sale in the territory licensed to Nycomed. Nycomed will pay DURECT blended royalties on sales in the defined territory of 15-40% depending on annual sales, as well as a manufacturing mark-up. DURECT retains full ownership of POSIDUR in the U.S., Canada, Asia and other countries.

About DURECT Corporation

DURECT Corporation is an emerging specialty pharmaceutical company developing pharmaceutical systems based on its proprietary drug delivery platform technologies. The Company currently has a number of late-stage pharmaceutical products in development addressing large markets in pain management, with a number of research programs underway targeting chronic disease and other therapeutic areas. For more information, please visit http://www.www.durect.com.

DURECT Forward-Looking Statement

The statements in this press release regarding POSIDUR, its potential performance and attributes, our anticipated end-of-Phase II meeting with the FDA and future development plans for POSIDUR and our intended emergence as a specialty pharmaceutical company are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, Nycomed and our abilities to design, enroll, conduct and complete clinical trials, obtain successful results from such clinical trials, complete the design, development, and manufacturing process development of POSIDUR, obtain regulatory and manufacturing approvals from regulatory agencies, and manufacture and commercialize POSIDUR, as well as marketplace acceptance of POSIDUR. Further information regarding these and other risks is included in DURECT's Form 10-Q dated May 9, 2007 under the heading "Risk Factors."

NOTE: POSIDUR(TM) and SABER(TM) are trademarks of DURECT Corporation. POSIDUR is under development and has not been submitted or approved for commercialization by the FDA or other health authorities.

SOURCE DURECT Corporation
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