Press Release

FDA Approves Shared REMS (Risk Evaluation and Mitigation Strategy) Program for all TIRF (Transmucosal Immediate Release Fentanyl) Pain Treatments

New Shared System Follows Model of REMS Program Pioneered by ProStrakan with the launch of ABSTRAL® (fentanyl) sublingual tablets

Bedminster, NJ, December 30, 2011 — ProStrakan, Inc., a subsidiary of Kyowa Hakko Kirin Co. Ltd. (KHK), and an international specialty pharmaceutical company, today announces that the U.S. Food and Drug Administration (FDA) has approved the TIRF (Transmucosal Immediate Release Fentanyl) REMS (Risk Evaluation and Mitigation Strategy) Access program. This new REMS is a single shared system for all TIRF products, including ABSTRAL® (fentanyl) sublingual tablets, an opioid analgesic used in the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.

The goals of the TIRF REMS Access program are to mitigate the risk of misuse, abuse, addiction, overdose and serious complications due to medication errors by:

- Prescribing and dispensing TIRF medicines only to appropriate patients, which includes use only in opioid-tolerant patients.
- Preventing inappropriate conversion between fentanyl products.
- Preventing accidental exposure to children and others for whom it was not prescribed.
- Educating prescribers, pharmacists and patients on the potential for misuse, abuse, addiction and overdose of TIRF medicines.

TIRF products are available only through REMS programs, which require enrollment by prescribers, their patients, pharmacies and distributors. Today, TIRF manufacturers have separate REMS programs and a health care provider and pharmacy must enroll in multiple REMS programs, corresponding to the TIRF product they choose to prescribe or dispense. The new shared REMS – modeled after the program created for ABSTRAL - will go live in March 2012; at that time, prescribers, pharmacies, patients, and distributors may all be enrolled in a single program for these products. All stakeholders currently enrolled in any of the individual REMS programs will be automatically enrolled in the shared system in March 2012.

"ProStrakan is thrilled to see our hard work and the work of the industry working group culminate in this approval," said Anthony G. Oladipo, Pharm.D., M.P.H, BCPS, VP Global Head of Drug Safety & Risk Management, ProStrakan, Inc. "We are fully committed to patient safety and pleased to help the FDA achieve its goal of assuring appropriate use of pain medications."

ProStrakan's product, ABSTRAL is the first and only rapidly-disintegrating tablet placed under the tongue for breakthrough cancer pain. In January 7, 2011 it was approved by the FDA for use in cancer patients, 18 years of age or older, who are already receiving, and who are tolerant to, opioid therapy for their underlying persistent cancer pain.

"ABSTRAL provides a simple, patient-friendly and efficacious treatment option for cancer patients with breakthrough pain, which can be incapacitating, limiting patients' ability to participate in daily activities," said John Higgins, General Manager, ProStrakan, Inc. "Now, all TIRF products will be administered equally through a single REMS, making the process simpler for prescribers, patients, pharmacists, and distributors."

Breakthrough cancer pain, common in up to two-thirds of people with cancer-related pain, affects a patient's quality of life, including physical and emotional health, interpersonal relationships and the ability to engage in certain activities. Breakthrough pain (BTP) is described as severe pain that "breaks through" the patient's round-the-clock pain medicine.[i] Opioids are among the most potent and effective analgesics, or medicines given to reduce pain, but unfortunately are also some of the most misused and abused medicines.

For more information on ABSTRAL, please visit www.ABSTRAL.com. For more information on the TIRF REMS Access program, please visit www.TIRFREMSAccess.com or call 1-866-822-1483.

About ABSTRAL®

ABSTRAL® (fentanyl) sublingual tablets, a rapidly disintegrating sublingual tablet formulation of fentanyl citrate designed for oral transmucosal delivery, is approved in the U.S. for the management of breakthrough pain in cancer patients 18 years of age or older who are already receiving, and who are tolerant to, opioid therapy for their underlying persistent cancer pain. ABSTRAL is available in strengths of 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg. ABSTRAL offers an alternative therapeutic choice to patients and clinicians with a simple, patient-friendly and predictable way of delivering fentanyl transmucosally, while retaining the individualized dose titration aspects required for optimal treatment of breakthrough pain.

ABSTRAL is in-licensed by ProStrakan for Europe, the U.S., Canada, and Mexico from Sweden-based Orexo AB.

Important ABSTRAL® Safety Information

IMPORTANT:
Do not use ABSTRAL unless you are regularly using another opioid pain medicine around-the-clock for your cancer pain and your body is used to these medicines (this means that you are opioid tolerant).

Keep ABSTRAL in a safe place away from children.
Get emergency medical help right away if:

- **a child takes ABSTRAL. ABSTRAL can cause an overdose and death in any child who takes it.**
- **an adult who has not been prescribed ABSTRAL takes it**
- **an adult who is not already taking opioids around-the-clock, takes ABSTRAL**

These are medical emergencies that can cause death. If possible, try to remove ABSTRAL from the mouth.

ABSTRAL can cause life-threatening breathing problems that can lead to death. Breathing problems are more likely to occur in patients with underlying breathing problems, elderly patients, or impaired or weak patients. These problems usually occur after large initial doses in patients who are not opioid tolerant or when opioids are given with other medicines that that slow breathing.

ABSTRAL is made with the prescription medicine fentanyl. Your healthcare provider will prescribe a starting dose of ABSTRAL that may be different than other fentanyl-containing medicines you may have been taking. Do not switch from ABSTRAL to other medicines that contain fentanyl without talking with your healthcare provider.

ABSTRAL is a federally controlled substance (CII) because it is a strong opioid (narcotic) pain medicine that can be misused by people who abuse prescription medicines or street drugs.

Never give ABSTRAL to anyone else, even if they have the same symptoms you have. It may harm them or cause death.

Do not take ABSTRAL for short-term pain that you would expect to go away in a few days, such as pain after surgery, headache, migraine, or dental pain.

Do not take ABSTRAL if you are allergic to any of the ingredients in ABSTRAL.

Tell your doctor about all of your medical and mental health problems. If you have trouble breathing or lung problems such as asthma, wheezing, or shortness of breath, ABSTRAL may cause more serious breathing problems.

Do not take any medicine while using ABSTRAL until you have talked to your healthcare provider. Be very careful about taking other medicines that may make you sleepy, such as other pain medicines, anti-depressants, sleeping pills, anti-anxiety medicines, antihistamines, or tranquilizers. Also, do not drink alcohol while using ABSTRAL.

Do not drive, operate heavy machinery, or do other dangerous activities until you know how ABSTRAL affects you. ABSTRAL can make you sleepy. Ask your healthcare provider when it is ok to do these activities.

ABSTRAL is only available through a program called the ABSTRAL REMS program. To receive ABSTRAL, you must talk to your healthcare provider, understand the benefits and risks of ABSTRAL, agree to all of the instructions, and sign the Patient-Prescriber Agreement form.

You or a family member should call your healthcare provider or get emergency medical help right away if you:

- Have trouble breathing
- Have drowsiness with slowed breathing
- Have shallow breathing (little chest movement with breathing)
- Feel faint, very dizzy, confused, or have other unusual symptoms

These symptoms can be a sign that you have taken too much ABSTRAL or the dose is too high for you. These symptoms may lead to serious problems or death if not treated right away. If you have any of these symptoms, do not take any more ABSTRAL until you have talked to your healthcare provider.

ABSTRAL can cause your blood pressure to drop. This can make you feel dizzy or lightheaded if you get up too fast from sitting or lying down.

The most common side effects of ABSTRAL are nausea, sleepiness, and headache.

Constipation (not often enough or hard bowel movements) is a very common side effect of pain medicines (opioids) including ABSTRAL. Talk to your healthcare provider about dietary changes, and the use of laxatives (medicines to treat constipation) while you are taking ABSTRAL.

Please see full Prescribing Information and Medication Guide, including Boxed Warning.

About ProStrakan

ProStrakan is a rapidly growing specialty pharmaceutical company engaged in the development and commercialization of prescription medicines for the treatment of unmet therapeutic needs in major markets.

ProStrakan is a subsidiary of Kyowa Hakko Kirin Co. Ltd., the Japan-based global specialty pharmaceutical company.

ProStrakan's head office is located in Galashiels, Scotland. The company's development capabilities are centered in Galashiels and Bedminster, New Jersey, U.S. Sales and marketing of ProStrakan's portfolio of products are handled by commercial subsidiaries in the UK, U.S., France, Germany, Spain, Italy and other EU countries.

You can learn more about the business at: www.prostrakan.com

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Contact:

Glenn Silver
SharedVoice Public Relations
+1 (212) 884-0646

Callum Spreng
ProStrakan Corporate Communications
+44 (0)1896 664000

[i]Portenoy RK, Hagen NA. Breakthrough pain: definition, prevalence and characteristics. *Pain*. 1990;41: 273-281.