

PL-3994 for Congestive Heart Failure Indications



PALATIN
TECHNOLOGIES, INC.

ABOUT PL-3994

PL-3994, discovered and developed by scientists at Palatin Technologies, is a natriuretic peptide receptor A (NPRA) agonist compound. Developed for treatment of both acute congestive heart failure (CHF) and chronic heart failure, PL-3994 has successfully completed both a Phase 1 and Phase 2a trial.

Unlike recombinant natriuretic peptides, PL-3994 is a synthetic molecule, incorporating a novel and proprietary amino acid mimetic developed by Palatin Technologies. PL-3994 has an extended half-life, with reduced affinity for natriuretic peptide clearance receptors and increased resistance to neutral endopeptidase, an endogenous enzyme that degrades natriuretic peptides. The result is a drug with improved pharmacokinetic and pharmacodynamic properties.

PL-3994 is one of a library of natriuretic peptide receptor agonist compounds developed by Palatin Technologies. Broad patent applications have been filed in the United States and internationally, protecting this family of novel compounds. Based on priority dates, patent protection will extend through 2026, and may be eligible for patent term extensions.

What is Heart Failure?

Heart failure is a cardiac disorder that impairs the ability of the heart to pump sufficient blood through the body. It is associated with an annual mortality of 10%.

PL-3994: Preclinical Development

Unlike other natriuretic peptide drugs, all of which are intravenously administered, PL-3994 has been developed as a subcutaneously administered drug. The subcutaneous format permits precise control of dosing. PL-3994 is formatted for administration by patients, like insulin and similar drugs.

Preclinical studies in animals established a dose-dependant effect on blood pressure and urine production (diuresis), and in animal models of congestive heart failure showed improved kidney function and prevention of cardiac hypertrophy (increase in heart size due to disease). Safety toxicology studies were conducted in animals prior to filing an Investigational New Drug application with the Food and Drug Administration.

PL-3994: Clinical Trials

The Phase 1 trial was a randomized, double-blind, placebo-controlled, study in 26 healthy volunteers who received either PL-3994 or placebo subcutaneously. Evaluations included safety, tolerability, pharmacokinetics and several pharmacodynamic endpoints, including levels of cyclic guanosine monophosphate (cGMP), a natural messenger nucleotide. Dosing concluded with the successful achievement of the primary endpoint of the study, a prespecified reduction in systemic blood pressure. No volunteer experienced a serious or severe adverse event. Elevations in plasma cGMP levels, increased diuresis (urine excretion) and increased natriuresis (sodium excretion) were all observed for several hours after single subcutaneous doses.

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A Phase 2a trial was conducted in volunteers with controlled hypertension who were receiving one or more conventional antihypertensive medications. In this trial, which was a randomized, double-blind, placebo-controlled, single ascending dose study in 21 volunteers, the objective was to demonstrate that PL-3994 can be given safely to patients taking antihypertensive medications commonly used in heart failure and hypertension patients. Dosing concluded with the successful achievement of the primary endpoint of the study, a prespecified reduction in systemic blood pressure. No volunteer experienced a serious or severe adverse event. Elevations in plasma cGMP levels were observed for several hours after single subcutaneous doses.

Palatin intends to develop PL-3994 for use in patients with chronic heart failure who suffer a decompensation requiring hospitalization. The medication will be continued following hospital discharge to reduce the rate of rehospitalization. This is a major unmet medical need since as many as 30% of patients are rehospitalized in the months after inpatient treatment for their heart failure. Palatin will discuss this approach with the Food and Drug Administration in the second quarter of 2009, with further Phase 2 trials to be initiated thereafter.

PL-3994: Market Potential in CHF

Over 5 million Americans suffer from CHF, with 550,000 new cases of CHF diagnosed each year –statistics that will only increase with the aging of the American population. Despite the treatment of CHF with multiple drugs, almost all CHF patients will experience at least one episode of worsening CHF that requires treatment with intravenous medications in the hospital. Congestive heart failure has tremendous human and financial costs. Estimated direct costs in the U.S. for CHF were \$29.6 billion in 2006.

Market Opportunity

CHF is the leading cause of hospitalization in people over 65 years of age, with over 1,100,000 hospitalizations for CHF in 2004. CHF is also a high mortality disease, with approximately 50% of CHF patients dying within five years of initial diagnosis.

PL-3994: Opportunities and Competition

PL-3994 is a novel NPRA agonist compound with very favorable properties for drug development. It increases cGMP levels in vascular smooth muscle, a pharmacological response well suited for treating CHF. PL-3994 increases both diuresis and natriuresis, at least in part by decreasing activity of the renin-angiotensin-aldosterone system ("RAAS"), a hormone system that regulates blood pressure and water (fluid) balance. Thus PL-3994 causes decreases in both systolic and diastolic blood pressure.

PL-3994 is well absorbed through the subcutaneous route of administration. The pharmacokinetic half-life in animals is about two hours, with a pharmacodynamic half-life in human studies of about three hours.

One natriuretic peptide is currently marketed in the United States, Natrecor® (nesiritide), a recombinant human B-type natriuretic peptide (BNP). This product is approved only for intravenous infusion for treatment of acute decompensated CHF, and because of its very short half-life (approximately 18 minute elimination half-life) is unlikely to be suitable for subcutaneous administration or for treatment of chronic CHF. While PL-3994 may compete with Natrecor for treatment of acute CHF in a hospital setting, there is no NPRA agonist drug approved in the United States for treatment of chronic heart failure, including worsening heart failure. Subcutaneously injectable PL-3994, a format permitting self-administration by the patient, is intended to address this critical unmet medical need.

The statements in this Fact Sheet that relate to future plans, events or performance are forward-looking statements, which are made pursuant to the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934. Such forward-looking statements involve significant risks and uncertainties, and actual results, events and performance may differ materially from those expressed or implied in this Fact Sheet. Factors that could cause such differences include, but are not limited to, risks pertaining to product development, clinical trial outcomes, regulatory requirements and actions, availability of required financing and other sources of funds, corporate partnering agreements and other risks disclosed in the our most recent Annual Report on Form 10-K and other periodic reports filed with the Securities and Exchange Commission. The forward-looking statements in this presentation do not constitute guarantees of future performance. We undertake no obligation to publicly update these forward-looking statements to reflect events or circumstances that occur after the date of this Fact Sheet.

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