

pulmatrix: IMPROVING PATIENT OUTCOMES WITH 'INHALED' THERAPIES

Pulmatrix's iSPERSE™ technology shows signs of being a key advance in delivering drugs into the lungs, offering major medical benefits to patients with lung disease.

For Robert Clarke, PhD, and his Lexington, MA based pharmaceutical company, Pulmatrix, Inc. (NASDAQ: PULM), the crucial moment came in 2010. Pulmatrix researchers had previously discovered that inhaling certain salts in liquid aerosols into the lungs could cut risks of contagion after a biological weapons attack—and that those aerosols could also fight inflammation in the lungs.

So company scientists began experimenting with a way to turn the liquid aerosol into a dry powder. Dry powders are more portable and faster to inhale, which is advantageous to dosing patients. The R&D team turned to a familiar process, spray-drying, a process whereby the ingredients are dissolved in a solution, the liquid forced through a jet nozzle to form droplets which are then quick dried resulting in dry particles.

Working at the Massachusetts Institute of Technology back in the mid-1990s, one of Pulmatrix's founders, David Edwards (now a professor of bioengineering at Harvard), originally had a key insight for using spray-drying to solve the challenge of effectively getting dry powders into patient airways by inhalation. He realized that particles would fly better if they were light and airy, like a whiffle ball instead of a heavy baseball.

Pulmatrix followed up on that insight in and a new platform technology was born. The company developed its patented iSPERSE™ technology, which makes tiny particles that look a bit like raisins, with lots of nooks and crannies. Almost counterintuitive to Dr. Edwards' earlier discovery, iSPERSE particles are dense



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but “require very little energy to make them fly because they don't stick together,” Dr. Clarke explains.

The results of those experiments “were a complete surprise,” Dr. Clarke recalls. Not only could the researchers engineer particles that fly easily into the small airways of the lung despite a density profile that might suggest otherwise, they also could include many different types of drugs in the particles.

Clarke realized that Pulmatrix had suddenly made a major advance in tackling one of medicine's greatest challenges—efficiently delivering drugs to the lungs. Existing products



(nebulizers, metered dose inhalers, and lactose blend dry powder inhalers) for lung diseases like asthma and chronic obstructive pulmonary disease (COPD) all have limitations, such as leaving too much drug behind in the delivery device or stuck in the throat rather than delivering it to the lungs. They are also limited in the types of drugs they can deliver based on chemistry and dose.

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Over the next two years, the company determined that iSPERSE could formulate a variety of drugs, from small molecules to large antibodies, and began looking for opportunities to bring products to market quickly for patients in need.

So what drugs should Pulmatrix deliver with this powerful new method? Today, Pulmatrix is targeting important unmet medical needs and contemplating expedited regulatory paths by repurposing approved

drugs that iSPERSE will make much better. “Our current pipeline allows us to walk before we can run while building valuable products for patients,” explains Dr. Clarke. “Once we’ve matured the technology and gotten an approved product, there will be huge opportunities for going beyond what we’re doing now.”

The first opportunity in the company pipeline is developing a competitor to a once daily muscarinic antagonist, a type of bronchodilator for COPD that sells \$5 billion per year. “We thought we could make a better version,” Dr. Clarke explains. Because of iSPERSE’s advantages, “in a phase Ib study we were able to use 80% less of the drug in the product and get the same benefit in the patients’ airways,” says Clarke. The iSPERSE drug particles also fly so easily that COPD patients should be able to breathe them deep into the lungs even on their worst days when breathing itself is a struggle—an improvement over the lactose-blended current product.

A special speedy regulatory pathway in Europe just for inhaled COPD & asthma drugs could get the product, now called PUR0200, on the market in Europe earlier than is possible in the U.S., says Dr. Clarke. Pulmatrix already has disclosed a pharma partner who has an option on the EU rights to the program.

A second clear opportunity is in treating fungal infections for lung disease patients, an unmet medical need. Delivering the drug to the lungs directly should dramatically improve the lung tissue levels to treat the fungal infection “where it lives” and reduce side effects compared to the current oral drug, the company believes. The current treatment is oral drugs with a less-than-ideal dosing profile that can cause serious side effects because high doses are required to get enough drug to lung cells through the bloodstream. Delivery via the stomach to the bloodstream also raises significant concerns about adverse drug-drug interactions which can lead to contraindication—meaning certain

combinations of drugs can’t be used at the same time despite the patient need.

The inhaled drug, called PUR1900, also has great business potential. In addition to treating fungal infections for patients with lung disease like severe asthma or cystic fibrosis, it could also be developed to prevent fungal infections in people with compromised immune systems, comprising a total addressable patient population into the millions.

The branded generic bronchodilator product and the anti-fungal product are just the beginning for Pulmatrix. Company scientists are also developing inhaled therapeutics for idiopathic pulmonary fibrosis (IPF), a progressive and generally fatal disease. These products would also be a crucial medical advance with high market potential. And with enough cash on hand to last into mid-2017, past important milestones for the two lead clinical programs, Pulmatrix is well positioned to either bring these important products to market or attract a Big Pharma partner or buyer. “We see major opportunities ahead, both in making a difference in the lives of patients and in rapid growth for Pulmatrix,” says Dr. Clarke.

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