

PUR0200 for COPD

PUR0200 is a once-daily, inhalable iSPERSE™ reformulation of tiotropium bromide for COPD patients. PUR0200 is under development as a substitutable product for Spiriva® HandiHaler® in the European Union (EU) and as a branded alternative to Spiriva HandiHaler in the US.

In Europe, development follows the hybrid pathway for orally inhaled products based on PK bioequivalence with a targeted pivotal trial in 2018. In the United States, PUR0200 is following a 505(b)(2) development path.

PUR0200 Market Opportunity

PUR0200 is expected to compete for a share of the \$5.5B worldwide market. Despite the arrival of new combination therapeutics, GOLD guidelines designate LAMA as a first line COPD therapy, so continued growth is expected. Market exclusivity as a branded generic, reduced COGS, and a first-to-market alternative well ahead of traditional generics will support significant market penetration for PUR0200.

PUR0200 Differentiation

PUR0200 is formulated using Pulmatrix’s novel iSPERSE platform that is clinically proven to minimize throat deposition and reduce the nominal dose of API by 66-80% compared to the lactose blend products. These features result in an improved patient use profile and reduced COGS.

PUR0200 Development Highlights

Pulmatrix has completed two clinical trials of PUR0200 in support of PUR0200 bioequivalence to Spiriva HandiHaler.

A study in moderate to severe COPD patients showed that PUR0200 results in similar exposure to the reference product at 80% of the nominal dose. (Figure 1). This same dose results in the same bronchodilatory effect as Spiriva HandiHaler. (Figure 2). This suggests that PUR0200 can achieve matching exposure and lung function improvement at significantly lower patient exposure.

Systemic Exposure Comparison to Reference Product

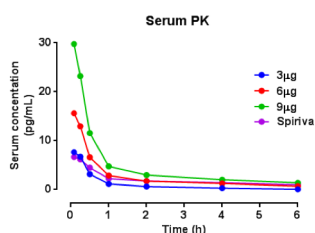


Figure 1. Plasma levels increase with single doses of PUR0200 and match kinetics to reference product in moderate to severe COPD patients. Similar exposure was achieved at 3 µg PUR0200 compared to 18 µg Spiriva HandiHaler.

Improved Lung Function in COPD Patients

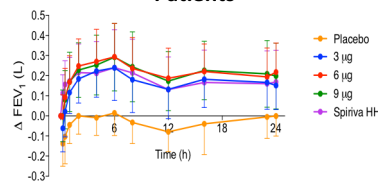


Figure 2. Single doses of PUR0200 significantly improved FEV₁ in moderate to severe COPD patients. The 3 µg PUR0200 results in similar peak and trough FEV₁ improvements as 18 µg Spiriva HandiHaler.

PUR0200 Equivalence to Spiriva HandiHaler

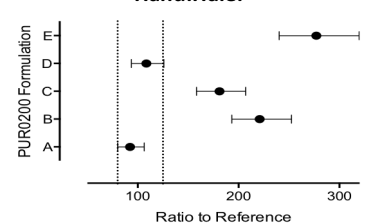


Figure 3. The C_{max} bioequivalence of 5 different PUR0200 formulations (A-E) was compared to Spiriva HandiHaler (acceptance criteria indicated by dashed lines). Two formulations met or nearly met bioequivalence criteria and identified drug product targets for the pivotal PK study.

PUR0200 Business Opportunity

- Streamlined Regulatory Path to EU \$1B Market:** Pulmatrix received positive feedback from the UK Medicines & Healthcare and Product Regulatory Agency (MHRA) and the Medical Products Agency (MPA) in Sweden, that PUR0200 can move directly to a pivotal PK bio-equivalence study for EU approval in 2018.
- Well Defined 505(b)(2) Regulatory Path to US \$4.5B Market:** iSPERSE platform allows flexibility of device selection and reduced nominal dose, providing an opportunity to develop a differentiated multi-dose delivery product on a 505(b)(2) path for US regulatory approval.
- Freedom to Operate and Limited Generic Competition:** Composition of matter patents for the reference product expired in 2016 (EU/UK) and will expire in 2018 (US). The reference product is further protected by patents for the physical form of the API and lactose blend specific process patents. The extended patent coverage block lactose blend generic competition into the late 2020’s. Using the iSPERSE platform, PUR0200 is engineered as a non-infringing product that does not involve lactose blending. These advantages support the launch of the first branded generic upon expiration of the composition of matter patents.
- Broad patent protection:** PUR0200 is protected by an extensive estate of intellectual property of more than 100 patents, including iSPERSE platform, product and method of use patents. Intellectual property coverage for PUR0200 extends into the 2030s with the recent grant of US Patent 9,642,798.