Fzata, Inc.
www.fzata.com

Bioengineered Probiotic Yeast Medicine (BioPYM): a first-in-class platform for oral live biotherapeutics

Bioengineered Probiotic Yeast Medicines are oral, live therapeutics that express and secrete disease-targeting therapeutic molecules in situ for the treatment of gastrointestinal-related diseases. This synthetic biology approach offers advantages over conventional protein biologics and fulfils the dream of oral administration.

The power of protein biologics to treat a range of diseases, including gastrointestinal (GI) disorders, is widely recognized—and so are their numerous drawbacks. Recombinant protein biologics are expensive and labor-intensive to manufacture and purify, and require refrigeration for transportation and storage. These difficulties are reflected in the price. Another disadvantage of protein biologics is that patients often receive such drugs by regularly attending clinics for intravenous infusions or by self-injection, since they are unsuitable to be taken orally.

Fzata, Inc. has created a first-in-class oral biologic modality that overcomes the limitations of conventional protein biologics for GI diseases. Bioengineered Probiotic Yeast Medicines (BioPYMs) are live biotherapeutic products (LBPs) formulated in a capsule to achieve the 'Holy Grail' of oral biologics. The platform leverages yeast as micro-factory to produce disease-targeting protein drugs, enabling the development of more potent biotherapeutics over natural microbiota approaches. BioPYMs are easy for patients to take at home, eliminating the need for inconvenient and time-consuming trips to receive their biologic medicine, a factor that contributes both to decreased compliance and to health inequalities, especially for those living in rural areas.

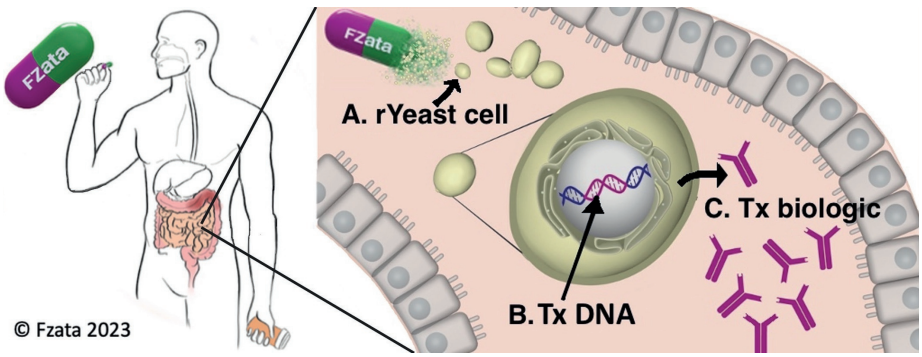

Fig. 1 | Bioengineered Probiotic Yeast Medicines (BioPYMs) in action. A, Orally administered, enteric-coated BioPYM capsule dissolves in the small intestine and releases live, lyophilized recombinant yeast (rYeast) cells. **B**, rYeast cells carry a chromosomal inserted gene encoding therapeutic protein. **C**, Disease-targeting therapeutic proteins are secreted during the yeast passage through the gastrointestinal tract; rYeast does not colonize the gastrointestinal tract, allowing for controllable drug pharmacokinetics.

The BioPYM platform: how it works

The BioPYM platform utilizes synthetic biology to create disease-targeting yeast *Saccharomyces boulardii*. Wild-type *S. boulardii* has known probiotic properties and is widely available in drug stores for improving gut health. With years of research and development effort, Fzata has innovated the BioPYM platform, which can produce DNA payloads encoding any kind of protein from small peptides to complicated antibody proteins in the gut. Lead proprietary BioPYM candidates deliver protein biologics having well-studied mechanisms of action and known efficacy for GI diseases as well as gut function modulation.

BioPYMs are packed as dry yeast into capsules that, once swallowed, release the live yeast cells into the intestine, where they secrete the therapeutic proteins encoded by the DNA insert (Fig. 1). The *S. boulardii* micro-factories cut out the expensive manufacturing and purification processes typically required for producing protein biologics. In addition, the dry yeast cells are stable and can be safely transported and stored at room temperature. The use of yeast cells as biologic-producing micro-factories has key benefits compared with other approaches that attempt the same with bacteria. First, as eukaryotes, yeast cells are closer to human cells and are more likely to produce functional human therapeutic proteins than prokaryotic bacteria. Secondly, BioPYMs, but not bacterial products, allow for concurrent use with antibiotics. Thirdly, eukaryotic yeast cells do not transfer antibiotic-resistance genes as bacterial vectors do, thereby avoiding escalation of the superbug crisis.

Candidates in development

The company's lead BioPYM, FZ002, is an investigational new drug (IND)-ready candidate targeting the antibiotic-resistant superbug *Clostridioides difficile*, which is the most prevalent cause of nosocomial infections in industrialized countries. The incidence of *C. difficile* infection (CDI) has been rising in recent years with more than 450,000 cases and 30,000 deaths annually in the United States alone and medical costs exceeding $4 billion. FZ002 secretes a super-potent tetra-specific antibody that neutralizes two major *C. difficile* toxins, TcdA and TcdB, that cause disease symptoms ranging from diarrhea to fulminant colitis and death. FZ002 has been demonstrated efficacious in multiple animal CDI models, including fulminant infection in hamsters.

Fzata's second most advanced candidate, FZ006, encodes a neutralizing antibody against tumor necrosis factor-α (TNFα) for the treatment of inflammatory bowel disease (IBD). Up to 30% of IBD patients lose their response to anti-TNFα drugs and new treatments are much needed, particularly ones that are safe and effective for chronic use. FZ006 has shown promising results in multiple preclinical models of IBD, including a very severe disease mouse model that was comorbid with CDI. Unlike other needle-injected biologics, oral FZ006 acts locally in the intestine where the disease occurs and does not induce anti-drug antibody (ADA) response, making it safe for chronic use and also eliminating the need for immune-suppressing drugs such as methotrexate that have severe long-term toxicities.

Fzata is poised to take FZ002 into clinical trials, with FZ006 to follow, and has additional BioPYM pipeline candidates in early development. The company welcomes discussions with investors who share its vision of expanding access to convenient, cost-effective biologic therapeutics and reducing current health inequalities surrounding today's biologics.

CONTACT
Elizabeth Smith, Chief Business Officer
Fzata, Inc.
Halethorpe, MD, USA
Tel: +1-240-904-5127
Email: elizabeth_smith@fzata.com