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PRESS RELEASE

Da Volterra Announces Positive Top-line Results from a Phase 2 Clinical Trial Evaluating DAV132 in 260 Patients

- **First clinical study evaluating DAV132 in patients**
- **Primary endpoint met: DAV132 was safe for use in hospitalized patients with several comorbidities and concomitant medications**
- **DAV132 protects gut bacteria from antibiotic damage and so potentially against *C. difficile* infection**

Paris (France), 11th of February, 2020 **– Da Volterra**, a clinical-stage biopharmaceutical company developing innovative products to protect the intestinal microbiota from the damaging effects of antibiotics, today announced positive top-line results from a Phase 2 clinical trial 'SHIELD' evaluating DAV132 in patients receiving fluoroquinolone antibiotics. DAV132, Da Volterra's lead candidate, is a novel, first-in-class, orally administered, colon-targeted adsorbent designed to protect the intestinal microbiota of patients against antibiotic-induced disruption.

SHIELD was a multicenter, randomized, parallel-group comparative trial in which 260 patients were recruited in 4 European countries (Germany, Romania, Bulgaria, and Serbia). The study was designed to investigate the safety and efficacy of DAV132, taken during antibiotic treatment, to protect the intestinal microbiota. The patients enrolled had a median age of 71 years and 96% of them had at least one chronic comorbidity. They received oral or intravenous fluoroquinolone antibiotics for the treatment of lower respiratory tract infections, complicated urinary tract infections or for prophylaxis of febrile neutropenia, for a mean duration of 7.5 days. They were randomized into two groups: to receive the antibiotic treatment only (standard of care) or the antibiotic treatment with DAV132 7.5 grams three times a day.

The study met its primary endpoint and demonstrated positive results with regards to biological markers of efficacy for prevention of *Clostridioides difficile (C. difficile)* infection.

- DAV132 was highly efficient in capturing antibiotics in the colon: it significantly reduced free fecal concentrations of fluoroquinolones, without affecting their plasma levels, and thus their efficacy to treat patients' underlying infections.
- DAV132 protected the intestinal microbiota from antibiotic-induced disruption (*change of Shannon diversity index from baseline to end of antibiotic treatment: p-value of difference between the two groups = 0.003*).
- In tests conducted in collaboration with Mark Wilcox, Professor of Medical Microbiology at Leeds Teaching Hospitals and University of Leeds, the feces obtained from the patients receiving DAV132 and fluoroquinolones were not permissive for the growth of *C. difficile*, *ex vivo*, whereas the bacteria could grow in feces from patients treated with fluoroquinolones alone (*relative proliferation of C. difficile in stools from baseline to end of antibiotic treatment: p-value of difference between the two groups = 0.0003*). This finding suggests that DAV132 is able to protect patients against antibiotic-induced *C. difficile* infection.
- DAV132 was safe for use in hospitalized patients with several comorbidities and concomitant medications. The proportion of patients with adverse events related to DAV132 and/or antibiotics (blinded assessment by an independent committee) did not differ significantly between treatment groups. Notably, DAV132 did not interfere with the treatment of patients'

infections or with the control of their underlying diseases, confirming the safety profile demonstrated in previous studies conducted in healthy volunteers.

- By design, this trial was not powered to demonstrate clinical efficacy of DAV132 for the prevention of *C. difficile* infection or antibiotic-associated diarrhea, but the data support the progression to a pivotal study. Clinical efficacy will be confirmed in the planned phase 3 study in patients at high risk of developing a *C. difficile* infection.

"Results of this study showed that DAV132 could be safely administered to protect patients' intestinal microbiota from antibiotic-induced disruption, thus limiting the risks of developing a C. difficile infection and getting colonized by antibiotic resistant bacteria", said Thomas Louie, Professor of Medicine at the University of Calgary in Alberta (Canada), and President of the Scientific Committee of the SHIELD study.

"We are very pleased with the results of this Phase 2 study providing a compelling demonstration that microbiota protection by DAV132 is a novel potential means of combatting the crisis of infection by antibiotic resistant bacteria. The study is of tremendous importance as it confirms that DAV132 can be safely administered in patients with several comorbidities and concomitant medications without risk of interfering with these medications." declared Annie Ducher, Chief Medical Officer at Da Volterra.

Da Volterra is now preparing for the initiation of a Phase 3 pivotal study in patients with severe underlying disease.

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About DAV132:

DAV132 is a novel, patented colon-targeted adsorbent developed to protect the intestinal microbiota from the damaging effects of antibiotics. Co-administered with antibiotics, DAV132 has demonstrated its ability to selectively and safely suppress antibiotic disruption of the intestinal microbiota in multiple clinical trials. In patients taking antibiotics, DAV132 is developed for the prevention of *Clostridioides difficile* infections, as well as for the prevention of intestinal colonization by multi-drug resistant organisms and their dissemination. It is also anticipated to provide a significant clinical benefit, in combination with antibiotics, in patients undergoing allogeneic hematopoietic stem-cell transplantation (HSCT) as well as cancer patients treated with immune checkpoint inhibitors. DAV132 aims at being the first product protecting against the clinical consequences of intestinal microbiota dysbiosis to be available for physicians and patients.

About Da Volterra:

Headquartered in Paris (France), Da Volterra is a clinical-stage biopharmaceutical company whose vision is to be a trusted and acknowledged leader in the microbiota field. Da Volterra develops novel strategies aimed at protecting the intestinal microbiota to address large unmet medical needs in the infectious disease, gastroenterology, oncology, and hemato-oncology spaces. https://davolterra.com

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