

Melinta Therapeutics Updates Pyrrolocytosine and Enhanced Macrolide Programs at ECCMID Showcasing Company's Structure-Based Drug Design

New Haven, Conn, April 21, 2017 -- Melinta Therapeutics, a privately held company developing novel antibiotics to treat serious bacterial infections, announced today that collaborators of the company have been invited to make a presentation on the company's development of a novel class of antibiotics called pyrrolocytosines during a moderated e-poster session. These compounds are based on a molecular scaffold that was rationally designed for high binding affinity to a site on the bacterial ribosome not exploited by other commercially available antimicrobials. By honing the scaffolds' shapes and polarities, Melinta scientists have created hundreds of pyrrolocytosine compounds that demonstrate potent activity against Gram-negative bacteria, do not share cross-resistance with current therapies and – in their best examples – are not impacted by efflux, a major problem with resistant Gram-negative bacteria. Four exemplars from the class, with a range of expected activities, were profiled in the laboratory of Dr. David Livermore at the National Infection Service in Public Health England. Results from *in vitro* studies of these four compounds against several multi-drug resistant (MDR) bacterial isolates will be reviewed during an e-poster session by his colleague, Dr. Anna Vickers.

The *in vitro* studies conducted by Dr. Livermore's team evaluated the four pyrrolocytosines (RX-04A, RX-04B, RX-04C and RX-04D) against 96 drug-resistant isolates of Gram-negative species, including *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* sp., *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. The study was conducted to test the strength of exemplar pyrrolocytosines as credible agents to treat so-called CRE (carbapenem-resistant Enterobacteriaceae) as well as to test their ability to treat multidrug-resistant *A. baumannii* and *P. aeruginosa*, where multiple efflux pumps conspire to make them resistant to many, if not all, antibiotics. The isolates featured many examples of beta-lactamases, including NDMs, KPCs, VIMs and IMPs. They also featured *mcr-1*, which means "mechanism of colistin resistance." This mechanism is worrisome because it renders ineffective the one antibiotic in the arsenal (colistin) that is considered the last line of defense. Unlike other studies, this one featured at least one isolate that had more than one resistance mechanism in addition to *mcr-1* in the isolate. The pyrrolocytosines showed promising activity against all isolates, with RX-04A demonstrating greater potency than the other compounds. The minimum inhibitory concentrations (MICs) of RX-04A ranged from 1-2 micrograms/mL against *A. baumannii*, *E. coli* and the Enterobacteriaceae and 1-4 micrograms/mL against *P. aeruginosa* isolates.

"We have a deep familiarity with the bacterial ribosome that is unique in the industry. We chose an unexploited site on the bacterial ribosome to build a new class of antibiotics and tune that class to get in and stay in tough bacteria," stated Erin Duffy, Ph.D., chief scientific officer of Melinta Therapeutics. "We are working to optimize one or more pyrrolocytosines with an aim to bring the first one into the clinic where we may better assess its safety and activity in combatting these serious, sometimes life threatening pathogens."

In addition, two posters will be presented describing Melinta's development of enhanced macrolides and the activity of these candidates against Gram-positive bacteria. Macrolides, such as azithromycin, erythromycin and clarithromycin, inhibit protein synthesis in bacteria by binding to a site on the bacterial ribosome. They are often used as first-line treatment for methicillin-resistant *Staphylococcus aureus* (MRSA) infections, but resistance to macrolides has escalated in the last two decades.



Melinta scientists have identified structural changes to the macrolide backbone that cause it to build into an adjacent binding site of the ribosome, gaining affinity away from known sites of resistance and thereby overcoming them. Four enhanced macrolides created by Melinta (RX-230, RX-5312, RX-6425 and RX-6567) were tested against resistant pneumococci and staphylococci, including MRSA isolates. Each demonstrated good potency against these bacteria, with the majority of MICs less than or equal to 2 micrograms/mL, including against strains that have been constitutively methylated and dimethylated.

Details of the pyrrolocytosine and macrolide presentations are as follows:

- E-poster EP0399 (abstract A5925): Activity of novel pyrrolocytosine protein synthesis inhibitors against multi-resistant Gram-negative bacteria, including carbapenemase producers and those with MCR-1. Session: New antibiotics – new approaches. Sunday April 23, 2017 at 1:30 - 2:30
- Poster P1317 (abstract A7033): Unique mode of action and non-induction of resistance by novel 14- and 15-membered macrolides. Session: New drugs against Gram-positives. Monday April 24, 2017 at 12:30 - 1:30
- Poster P1328 (abstract A7078): Atomic eyesight is key to design of enhanced macrolides with true robustness to target-based resistance. Session: New drugs against Gram-positives. Monday April 24, 2017 at 12:30 - 1:30

About ECCMID

ECCMID is the annual meeting of the European Society of Clinical Microbiology and Infectious Diseases and is being held April 22-25, 2017 in Vienna, Austria. It attracts approximately 10,000 participants, making it the largest European congress for the presentation and discussion of research in the fields of clinical microbiology and infection. The scientific program is a synthesis of current priorities in the fields of clinical microbiology and infection. The diagnosis, treatment, epidemiology and prevention of infectious diseases, as well as related basic microbiology, are addressed by leading scientists during keynote lectures, symposia, meet-the-expert sessions, educational workshops, as well as poster and oral sessions. For more information, visit www.eccmid.org.

About Melinta Therapeutics

Melinta Therapeutics, Inc. is dedicated to saving lives threatened by the global public health crisis of bacterial infections, through the development of novel antibiotics that provide new and better therapeutic solutions. Melinta has submitted NDAs to the FDA for the intravenous and oral formulations of its late-stage investigational antibiotic, Baxdela, for the treatment of acute bacterial skin and skin structure infections (ABSSSI). Baxdela is also being studied in Phase 3 clinical development for the treatment of community-acquired bacterial pneumonia (CABP). Melinta is committed to developing, through the application of Nobel Prize-winning science, a new class of antibiotics designed to overcome the multi- and extremely-drug-resistant pathogens for which there are few to no options, known collectively as ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter* species and *Escherichia coli*), which cause the majority of life-threatening hospital infections.

Melinta Therapeutics is privately held and backed by Vatera Healthcare Partners (www.vaterahealthcare.com) and Malin Corporation plc (www.malinplc.com) among other private investors. The company is headquartered in New Haven, CT with offices in Lincolnshire, IL. Visit www.melinta.com for more information.



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