
Presentations at this year’s Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Diego, California, highlighted recent progress in antibiotic and vaccine development. Highlights for us included presentation of clinical data from Paratek Pharmaceuticals (NasdaqGM: PRTK), Aradigm (NasdaqCM: ARDM), and Tetraphase (NasdaqGS: TTPH) on their respective antibiotic programs. In addition, Merck (NYSE: MRK) presented immunogenicity data from two preclinical models on its cytomegalovirus (CMV) vaccine candidate. VBI Vaccines (NasdaqCM: VBIV) is also developing a CMV vaccine candidate.

- **Paratek Reported Data on the In Vitro Potency of Omadacycline in Treating Bacterial Isolates Underlying Cases of ABSSSI, CABP, and cUTI.** Paratek reported *in vitro* data on the potency of omadacycline in treating a range of clinically-relevant bacterial isolates for acute skin and skin structure infections (ABSSSI), community-acquired bacterial pneumonia (CABP), and complicated urinary tract infections (cUTI). Omadacycline is a tetracycline derivative that has been designed to overcome the two known mechanisms of tetracycline bacterial resistance. The antibacterial activity of omadacycline and other comparator antibiotics was measured as the minimum inhibitory concentration needed to kill 50% (MIC50) or 90% (MIC90) of the bacteria load. Omadacycline had low MIC values against US and European isolates from 2010 and 2014. In addition, there was no observed MIC shift for omadacycline when treating drug-resistant bacterial isolates. This indicates that omadacycline is effective against the current microbiological environment and that existing resistance mechanisms may not affect omadacycline’s antibacterial activity.

- **Aradigm’s Liposomal Antibiotics Were Effective against M. Abscessus Infections.** Aradigm presented preclinical data on the efficacy of liposomally-delivered ciprofloxacin in treating lung infections in beige mice caused by *Mycobacterium abscessus*. This strain of mycobacteria is particularly virulent and is resistant to most commonly-used antibiotics due to its formation of biofilms. *M. abscessus* is responsible for a subset of non-tuberculosis mycobacterium (NTM) infections that are growing increasingly prevalent in individuals with compromised lung function. Aradigm has developed two inhaled formulation of ciprofloxacin: Lipoquin (inhaled ciprofloxacin; CFI) and Pulmaquin (dual-release inhaled ciprofloxacin; DRCFI). *Pulmaquin* is currently under evaluation in two Phase III studies for the treatment of serious lung infections in patients with non-cystic fibrosis bronchiectasis (non-CF BE). The current preclinical study tested whether *Lipoquin* or *Pulmaquin* could effectively treat lung infections caused by *M. abscessus* and builds on data showing efficacy against *M. avium*, another mycobacterium that can cause NTM infections.

Both *Lipoquin* and *Pulmaquin* led to a significant reduction in the bacterial load of *M. abscessus* in the lung compared to untreated controls (p<0.05). At 6 weeks, *Lipoquin* and *Pulmaquin* treatment resulted in bacterial loads of 1.4±0.5 x 10^5 and 3.0±0.4 x 10^5 colony-forming units (CFU), respectively, compared to 5.4±0.6 x 10^5 CFU in untreated controls. There was also a significant decrease from week 3 to week 6 with either *Lipoquin* or *Pulmaquin* treatment (p<0.05), indicating a progressive improvement over time. Free ciprofloxacin not encased in a liposome was not effective at reducing bacterial load at either time point. These results highlight the efficacy of Aradigm’s antibiotics against virulent strains underlying NTM infections and support clinical development of either *Lipoquin* or *Pulmaquin* for this indication.

- **Merck’s CMV Vaccine Induces Weaker Immune Response than Natural CMV Infection in Preclinical Studies.** Merck presented data on the efficacy of its cytomegalovirus (CMV) vaccine candidate, V160, in two preclinical studies. The V160 vaccine is a replication-deficient virus designed to safely induce a CMV-specific immune response. The efficacy of the V160 vaccine candidate was assessed with a 50% neutralization titer (NT50) assay. Following 3 vaccine administrations with a novel adjuvant, rabbit sera had an NT50 of roughly 2,600 and sera from non-human primates reached an NT50 of 1,900. For comparison, sera from seropositive humans had an NT50 of roughly 4,000, indicating that Merck’s CMV vaccine candidate generates a weaker immune response than the response to natural CMV infection.

The weak response raises questions about the vaccine’s capacity to prevent congenital CMV infections. An ongoing Phase I study testing the safety, tolerability, and immunogenicity of V160 in seropositive and seronegative women will provide an important indication of the vaccine’s potential.

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of efficacy in humans. A competing program from VBI Vaccines (NasdaqCM: VBIV), which is developing V1501A as a prophylactic CMV vaccine, has shown neutralizing titers greater than that observed following natural CMV infection. VBI plans to launch a Phase I study in the first quarter of 2016, which could establish best-in-class potency in humans.

■ Questions Remain about the Future of the Eravacycline cUTI Program following Disappointing Results. Tetraphase presented in vitro data demonstrating the potency of the antibiotic eravacycline against a range of clinically-relevant bacteria underlying intra-abdominal (IAIs) and complicated urinary tract (cUTIs) infections. cUTIs are currently treated with intravenous (IV) antibiotics in an inpatient setting due to a lack of effective oral options. Tetraphase is one of three companies developing both oral and IV antibiotic formulations to address this unmet medical need. Paratek’s omadacycline and MerLion’s (private) finafloxacin are also in development for this indication. Earlier this month, Tetraphase announced the failure of a Phase III trial testing eravacycline in the treatment of cUTIs. The trial results were a surprise to many in light of a positive interim analysis in April 2015 and the in vitro potency of the antibiotic. The company has successfully completed a Phase III trial evaluating eravacycline for the treatment of intra-abdominal infections and may choose to move forward only in this indication. Tetraphase has not yet announced plans on the future of the eravacycline program, but it is unlikely that the company will continue development for the cUTI indication.

Expected Upcoming Milestones

■ Q4 2015 – VBI files IND for VBI-1501A for CMV.
■ YE 2015 – Paratek initiates Phase III trial evaluating omadacycline for CABP.
■ Early 2016 – Paratek commences Phase Ib trial for omadacycline in UTI.
■ Q1 2016 – VBI initiates Phase I trial for VBI-1501A for CMV.
■ Mid-2016 – Completion of Aradigm’s ORBIT-3 and ORBIT-4 Phase III trials evaluating Pulmaquin in BE.
■ H2 2016 – Completion of Merck’s Phase I trial evaluating CMV vaccine candidate, V160.
■ Late 2016 – Data expected from Paratek’s ABSSSI Phase III trial for omadacycline.
■ 2016 – Data on Allergan and Paratek’s sarecycline from Phase III trials.
■ H2 2017 – Data expected from Paratek’s CABP Phase III trial for omadacycline.
■ 2017 – Potential NDA filing for Allergan and Paratek’s sarecycline.
■ 2017 – Completion of VBI’s Phase I study, which is anticipated to be 20 months in duration.
■ H1 2018 – NDA filing for Paratek’s omadacycline in ABSSSI and CABP indications.
■ YE 2018 – Potential FDA approval of Paratek’s omadacycline for ABSSSI and CABP.


Analyst Certification

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