Q&A SESSION WITH DAVID CIPOLLA

DAVID CIPOLLA, Vice President of Research, **Insmed**

David Cipolla recently joined Insmed as VP of Research. More on that soon. Prior to joining Insmed, David led the preclinical R&D, pharmaceutical sciences and intellectual property efforts at Aradigm Corporation in Hayward, California. Aradigm is a specialty pharmaceutical company specializing in the development of inhalation treatments for severe respiratory disease. Prior to joining Aradigm, David worked at Genentech, Inc. in the Pharmaceutical Research and Development Group (1988-1996). His research investigated the development and characterization of the delivery of protein aerosols to the airways, culminating with the approval of Pulmozyme® rhDNase for the management of cystic fibrosis in 1993. David also made contributions to a number of marketed antibody products including Herceptin® Trastuzumab indicated for breast cancer and Xolair® Omalizumab for asthma.

At Insmed, what are your main priorities at the inhalation field at the moment?

Our highest priority is to ensure that we have done everything possible to ensure that our inhaled liposomal amikacin product gets approved for at least the sickest patients with NTM lung infections. These patients have worsening quality of life, poor outcomes and nothing is approved to treat their lung infections. At the recent August FDA Advisory Committee meeting to discuss approval of this product, I was touched by the voice of the patients. The key theme was that they had no hope, and approval of this therapy would give them hope. Our priorities are of course to help the patients, and especially patients with orphan diseases who have limited treatment options. We would certainly be interested in finding additional treatments for patients with NTM and others battling serious rare diseases. We have also publicly shared that we are working on a once-daily formulation of a prodrug of treprostinil that may provide improved convenience for PAH patients. In addition, we have publicly shared that we have an oral formulation of a small molecule inhibitor of neutrophil serine proteases which is being studied in patients with non-CF bronchiectasis.

You are giving your talk on inhaled antibiotics at the conference. What are the main challenges you face in developing the therapy?

For inhaled antibiotics, the challenges are selecting the appropriate antibiotics for the specific patient population and that depends upon which pathogen is being targeted. The biggest issues with the existing approved inhaled antibiotics is that they are giving twice or three times daily and so are not convenient for patients, and they are often not well tolerated in some patient populations (causing cough or bronchospasm). So by developing a nanocarrier formulation with the appropriate drug release rate, it may address both of those issues. If the drug is released over a 24 hour period, it may enable once-daily administration which will improve patient convenience. The particulate formulation may improve tolerability while also providing drug targeting to the specific regions in the lung with the pathogens; e.g., macrophages to target NTM infections.

In your opinion, what are the most exciting developments coming out in the Inhalation and Respiratory market?

Over the past few decades, there have been major advances in inhaler device technologies to improve the reproducibility of administration and provide compliance feedback to the patient which may increase engagement. There are now many device options for the patient to choose from including jet nebulizers, mesh nebulizers, soft-mist inhalers, MDIs, and DPIs. Many of these come with the advanced features that track usage, train the patient to have optimum inhaler technique, and increase connectivity with their health care providers or other patients. Thus, if a new therapeutic is being evaluated in the clinic, these technology advances may inform on whether non-responders were compliant (implying the drug was not effective) or non-compliant (and not implicating the drug). As I discussed above, I am also excited by the use of novel formulation technologies like liposomes to improve the profile of the drug, to reduce side effects, improve tolerability and improve targeting to the pathogen.