

Door Pharmaceuticals executive summary

Door Pharmaceuticals is a discovery stage company focused on exploiting virus structural proteins, the building block of a virus particle, to develop specific and curative antivirals. Virus structural proteins have no human homologs and have multiple functions, providing specificity and amplifying their antiviral impact.

Door is focused on chronic Hepatitis B Virus (HBV) infection. Worldwide, HBV infects more than 250M people and leads to more than 800,000 deaths each year. In the United States there are up to 2M people with chronic HBV. Though there is a vaccine, it has no effect on those with chronic HBV. Because current therapeutics are not curative and so once started they are a lifelong therapy, patients and doctors are reluctant to begin therapy. Less than 10% of chronic HBV patients know they are ill and less than 20% of those (~5M people) are taking virus suppressive therapeutics. Nonetheless, HBV therapeutics are \$4.6B market. A curative treatment is predicted to expand the market.

The HBV core protein dimer (HBc) has structural and non-structural functions, making it a pivotal antiviral target. Door is developing molecules that dysregulate non-structural functions of HBc. As a structural protein, HBc assembles into a spherical complex to package the viral genome at one end of the viral lifecycle and, at the other end, to release viral DNA to infect a new cell. HBc structural activity has been shown to be an effective antiviral target with Capsid Assembly Modulators (CAMs), a small molecule technology partly developed by Door founder Adam Zlotnick. Thus far, CAMs have not been curative.

HBc non-structural roles are critical to HBV infection. Non-structural functions include installing the viral genome in newly infected cells and suppressing innate antiviral defenses. While CAM molecules specifically target the oligomeric form of HBc, Door small molecules specifically target the dimeric form of the molecule, a unique approach. Door molecules have shown the ability to modulate expression of HBV expression in infected cells as both agonists and antagonists.

A small molecule that can turn off transcription of viral DNA has the potential to turn off the virus, re-activate the innate and adaptive immune systems, and lead to a functional cure. This will change the lives of millions of people.

Door was founded by Adam Zlotnick who is also Door's CSO. Dr. Zlotnick is a co-founder of Assembly Biosciences (NASDAQ: ASMB). He is a Professor of Molecular and Cellular Biochemistry at Indiana University. He has co-authored over 150 papers, mainly on virus structure and assembly. He is a fellow of the AAAS and the American Academy of Microbiology. Door's drug discovery is driven by a team of experienced medicinal chemists, HBV virologists, and entrepreneurs.