



2011-2012 POCC Lecture Series

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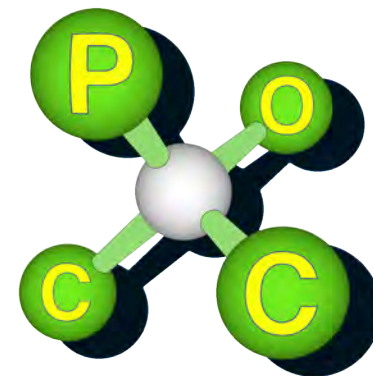
Dr. Jake M. Janey

Bristol-Myers Squibb

The Development of a Biocatalytic Manufacturing Process for Januvia®

Carolyn Hoff Lynch Lecture Hall
Chemistry Building, University of Pennsylvania

The Philadelphia
Organic Chemist's
Club

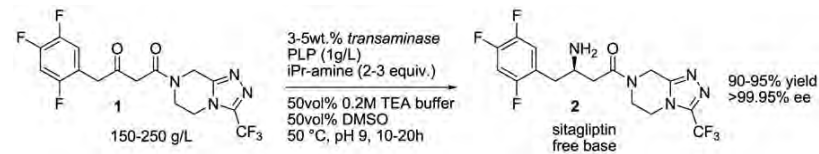


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Jake earned a Ph.D. from Harvard University under the mentorship of Prof. David Evans in 2003, where he studied chiral Lewis acid catalysis, including copper-catalyzed asymmetric cycloadditions of ketenes and chiral Salen-Aluminum complex-catalyzed asymmetric aldol reactions of aldehydes and 5-alkoxyoxazoles. He received a B.S. in chemistry from the University of Chicago, where he performed research on aminosiloxy diene Diels-Alder chemistry under the direction of Prof. Viresh Rawal.

Jake joined the Process Research group at Merck in 2003 where he impacted several late-stage projects including Merck's DPP IV compounds, telcagepant (CGRP), and Vaniprevir (HCV) programs. In 2007, Jake joined the Merck biocatalysis group, where he worked to combine the use of process chemistry, high throughput experimentation, and directed evolution (through a partnership with Codexis) to identify, optimize and evolve biocatalysts to broadly impact Merck's project pipeline. Jake also led the team that was responsible for the design, development, and implementation of a new manufacturing route for Januvia using a highly evolved transaminase enzyme.¹ This work was recognized by awards within Merck and by the Presidential Green Chemistry Award in that same year. In 2011, Jake moved to Bristol-Myers Squibb where he leads their efforts in the area of chemical automation applied to late stage chemical development efforts. Jake has authored sixteen journal publications and book chapters and is named on four patents.

Abstract: A new biocatalytic process using a highly evolved R-selective transaminase enzyme is described. This new manufacturing process was developed to replace the current catalytic, asymmetric enamine hydrogenation used to manufacture the anti-diabetic DPP-IV inhibitor sitagliptin, the active ingredient in Merck's Januvia®. Using a combination of "substrate walking" and a variety of directed evolution approaches, an industrial useful enzyme was produced starting from absolutely no activity in the parent transaminase. The resulting enzyme is not only capable of producing sitagliptin on industrial scale, but it has proven to be a broadly applicable catalyst towards the direct conversion of ketones to enantiopure R-amines. This work clearly demonstrates that biocatalysis is a mature, manufacturing ready technology with broad utility and application from discovery through commercial supply.¹



¹ C. K. Savile, J. M. Janey, et. al., *Science*, **2010**, 329, 305