

**Application of Transition-metal Catalysis and Biocatalysis as State-of-the-art Technologies in the Manufacture of a Key Intermediate of Entresto**

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Entresto® is a novel oral treatment for patients suffering from chronic heart failure that combines two active pharmaceutical ingredients – sacubitril as neprilysin inhibitor and valsartan as angiotensin II receptor blocker – in a single chemical entity. In contrast to valsartan, which has been an established API for already many years, a manufacturing process suitable for large-scale commercial production had to be developed for sacubitril. The use of both transition-metal catalysis and biocatalysis as state-of-the-art technologies was crucial to efficiently build up the molecular structure of sacubitril and achieve the defined performance targets required for the commercial manufacturing process.