PROCESS FOR PREPARING A GIP/GLP1 DUAL AGONIST

The present invention provides processes and intermediates for making a GIP/GLP1 dual agonist peptide, tirzepatide, or a pharmaceutically acceptable salt thereof.

Diabetes mellitus is a chronic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. In type 2 diabetes mellitus ("T2D"), the combined effects of impaired insulin secretion and insulin resistance are associated with elevated blood glucose levels. The GIP/GLP1 dual agonist, tirzepatide is described and claimed in United States patent 9474780 ("780 Patent"). Tirzepatide can be useful in the treatment of T2D.

US9474780 generally describes peptides and a method for making a GIP/GLP1 dual agonist.

There is a need for processes and intermediates to enable improved technology for production of tirzepatide having a combination of advantages including commercially desired purity. Similarly, there is a need for efficient and environmentally "green" processes, including stable intermediates to provide tirzepatide with fewer purification steps. Improved technology is also needed to provide tirzepatide manufacturing processes producing minimal waste streams for both environmental and operator enhanced safety. The preparation of large-scale, pharmaceutically-elegant tirzepatide presents a number of technical challenges that may affect the overall yield and purity. There is a need for processes to avoid the use of transition metals and/or harsh reaction conditions that are incompatible with peptide synthesis.

Summary

In an aspect of the present disclosure, there is provided a compound of SEQ ID NO:17, or a pharmaceutically acceptable salt thereof.

Description

The present invention seeks to meet these needs by providing novel intermediates and processes useful in the manufacture of tirzepatide (SEQ ID NO:1), or a pharmaceutically acceptable salt thereof. The improved terzepatide manufacturing processes of the present invention provide intermediates and process reactions embodying a combination of advances, including an efficient route having fewer steps, while at the same time maintaining high quality and purity. Importantly, the improved processes and intermediates decrease resource intensity and minimize waste streams.

The improved processes described herein provide various embodiments of intermdiates useful for production of terzepitide.

The present invention provides a compound of SEQ ID NO:17, or a pharmaceutically acceptable salt thereof. The present invention provides a compound of

WE CLAIM:

1. A compound of SEQ ID NO:17, or a pharmaceutically acceptable salt thereof.