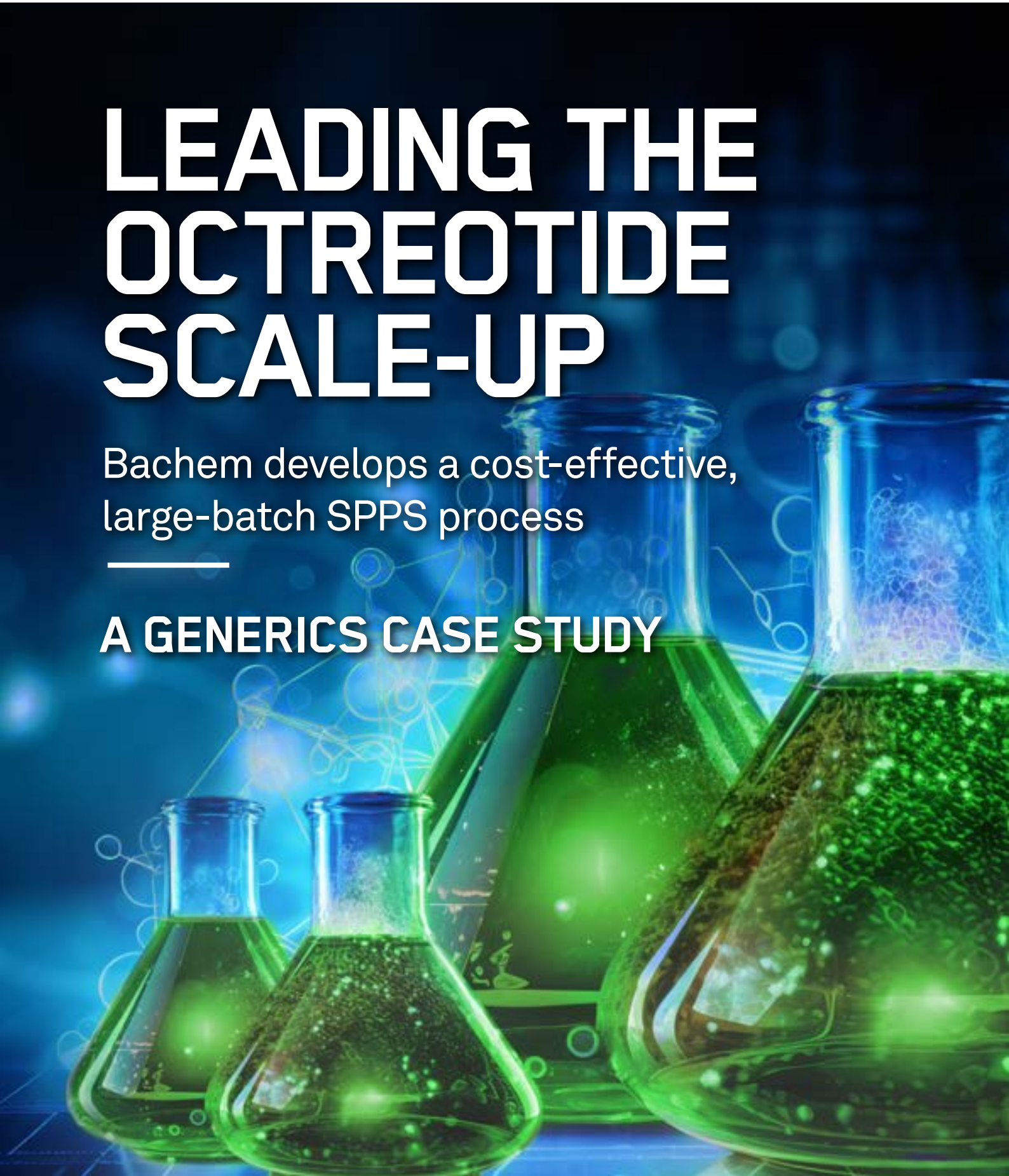
BACHEM

LEADING THE OCTREOTIDE SCALE-UP

Bachem develops a cost-effective, large-batch SPPS process

A GENERICS CASE STUDY



Octreotide acetate is a therapeutic octapeptide analog of the naturally occurring hormone somatostatin. First approved for use in the United States in 1988, this longer-acting synthetic peptide agonist is used for the reduction of growth hormone and insulin-like growth factor 1 primarily used in adults with acromegaly. 95% of acromegaly cases are caused by tumors of the pituitary gland where surgical resection is often not possible, requiring life-long use of growth hormone (GH)-lowering therapy. Challenges with pharmacological treatments include persistence of symptoms and failure of biochemical control, as well as therapy regimens requiring daily injections. GH-lowing therapy is associated with reduced quality of life (QOL) and higher economic burdens for patients. New therapies such as oral formulations promise better disease control and quality of life for patients but require 30-60 times higher octreotide acetate concentrations, thus putting demand on complex API manufacturers such as Bachem to cost-effectively scale production. Our client, a large pharmaceutical company who once manufactured octreotide in-house, decided in 2016 to partner with Bachem to take over large-scale API production. A win-win collaboration.

How to make complex peptides at quality and scale

Octreotide acetate is an active pharmaceutical ingredient (API) and synthetic somatostatin analog used for the treatment of acromegaly. The cyclic octapeptide is on the "List of Essential Medicines" published by the World Health Organization with a global market of around 1.4 Billion USD currently. US patent protections for octreotide expired in June 2014, albeit the patent has been challenged by generics competitors starting in 2005. New oral formulations promise improved quality of life for patients compared to daily or weekly injections but require 30-60 times higher API concentration, putting pressure on supply, cost, and generics competition.

In this case study, we highlight the history, process development, analytics, and regulatory services for octreotide acetate large-scale production at Bachem.

This case study also addresses a specific question: Our client gave up an established in-house manufacturing process and partnered with Bachem. Has their trust been rewarded?

A short timeline of upscaling octreotide acetate synthesis

When our client approached Bachem with the desire to scale up production, there was no Octreotide acetate process at Bachem Bubendorf, Switzerland. A GMP development process started promptly with the first 150 L reactor test production, using ~3 kg of 2-CTC resin. Raw purity after SPPS was around 80 % for SPPS and final purity reached 99.3% in March 2017.

After methodically implementing several confidential optimization steps in process innovation over the subsequent months, Bachem was confident up-scaling to a 1000 L SPPS reactor, initially with ~15 kg of 2-CTC resin, with the first batch having about ~99.9% purity in February 2018.

The first process performance quantification (PPQ) batch for authorities was produced with a purity of 99.8% in January 2019, followed by two more PPQ batches following in March and August of 2019, with purity exceeding 99.9% and 99.9%, respectively.

Total purity requirements are above 98.5%. Each unspecified impurity over 0.10% is reported. Our most recent large batches in March 2023 exhibited a purity of over 99.99% (impurities below detection limit), which is unmatched by other manufacturers.

MANUFACTURING COMPLEX APIS COST-EFFECTIVELY AT UNMATCHED SCALE AND HIGHEST QUALITY IS NOT JUST A CHALLENGE...

IT'S WHAT WE DO BEST

READ THE FULL CASE STUDY CLICK HERE