MASTERING THE SUPPLY CHAIN

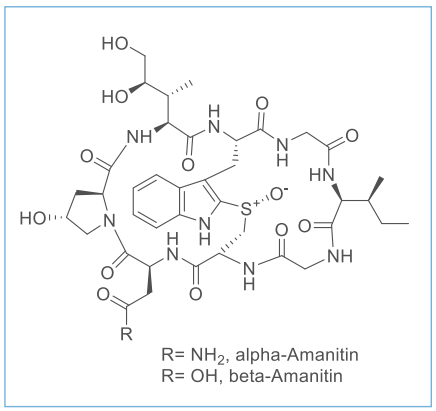
CARBOGEN AMCIS
A Dishman Group Company

A PROJECT THAT IS MUSHROOMING

After intense research investigations Heidelberg Pharma found a unique access to a fully synthetic route for α-Amanitin. With CARBOGEN AMCIS, Heidelberg Pharma developed a scalable and economical route providing α-Amanitin now available for the development of new therapeutic ADC's.

DISCOVERING A NEW ADC

The cyclic peptide α-Amanitin and analogue amatoxins have been investigated for over sixty years mostly by extraction from death cap mushrooms of the species *Amanita phalloides*. α-Amanitin is a highly selective and potent inhibitor of eukaryotic RNA polymerase II. Interaction of α-Amanitin with the RNA polymerase II bridge helix blocks the normal transcription processes of the cell, thus leading to cell apoptosis. This unique cellular mode of action makes α-Amanitin and related amatoxins ideal toxic payloads for antibody drug conjugates (ADCs). α-Amanitin ADCs have already shown outstanding antitumoral activity at low micrograms toxin doses in several malignant cancer cell lines from different origins. Despite such exceptional biological activity and pharmacological potential, the total synthesis of α-Amanitin and related compounds still remain a very challenging task, due to unique structural features.



Heidelberg PHARMA

HIGHLY POTENT CONTAINMENT

3X BUILDING BLOCK SYNTHESIS — MANCHESTER SITE
PR&D and non-GMP manufacture in EU
Lab scale, pilot scale, large scale manufacturing capacity up to 4'500 L

SOLID PHASE TRANSFORMATION — NEULAND SITE
PR&D and cGMP manufacture in EU and China
Lab scale, pilot scale, large scale manufacturing capacity up to 6'300 L

CHROMATOGRAPHIC SEPARATION — AARAU SITE
Preparative chromatography expertise
Up to 45 cm HPLC column separation
Up to 15 cm HPLC column separation for highly potent compounds

CONVERSION TO PAYLOAD — BUBENDORF SITE
4 sites for highly potent PR&D and cGMP manufacture
Up to 6'300 L for OEB 4 material
Up to 850 L for OEB 5 material

ANTIBODY CONJUGATION — BUBENDORF SITE
PR&D and cGMP bio-conjugation expertise
Up to 200 g ADC batch size

FILL AND FINISHED FORMULATION — RIOM SITE
Aseptic fill & finish
Liquid / Lyophilized filling up to 5000 vials

MASTERING THE SUPPLY CHAIN: FROM CHEMISTRY TO PATIENT