

Switzerland - The Country of Pharmaceuticals - Answer Sheet

| 6% of total | | | | | | | | |
|-------------|------|------|------|------|------|------|------|-------|
| Question | 10.1 | 10.2 | 10.3 | 10.4 | 10.5 | 10.6 | 10.7 | Total |
| Points | 2 | 11 | 6 | 6 | 6 | 6 | 2 | 39 |
| Score | | | | | | | | |

10.1 (2 pt)

Determine the number of stereogenic centers (n) in Pasireotide (**1**). **Calculate** the total number of all possible stereoisomers (t) of Pasireotide (**1**).

 $n =$ _____ $t =$ _____

10.2 (11 pt)

Draw reagents **A** and **D** and intermediates **B** and **C** in the synthesis of Fmoc-Tyr(Bn)-OH.

A

B

C

D

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10.3 (6 pt)

Choose the linker(s) **4** that are appropriate for SPPS of peptide **2** according to **Scheme 1** in the question sheet. Incorrect answers will result in deductions of points but the total score may not be negative.

- 2-Chlorotrityl-chloride linker (**a**)
- Safety-catch linker (**b**)
- Rink amide linker (**c**)
- SASRIN-chloride linker (**d**)
- Sieber amide linker (**e**)
- Wang linker (**f**)

10.4 (6 pt)

Choose the most suitable side-chain protecting groups **PG-1** and **PG-2** for SPPS of **2** according to **Scheme 1** in the question sheet that can be orthogonally cleaved in the presence of all other functional groups present in Pasireotide. Only one answer is correct for each of the protecting groups.

PG-1

- **g**
- **h**
- **i**
- **j**
- **k**
- **l**

PG-2

- **g**
- **h**
- **i**
- **j**
- **k**
- **l**

10.5 (6 pt)

Choose the correct statement(s) about the cyclization of peptide **2** to **8**. Incorrect answers will result in deductions of points but the total score may not be negative.

- A possible side-product of the reaction is tetramethylguanidylolation of the N-terminal phenylalanine residue resulting in compound **9**.
- A possible side-product of the reaction is the cleavage of protecting group **PG-1** and cyclization via the amino group of the lysine residue to give compound **10**.
- The reaction must be carried out at a high peptide concentration to achieve a sufficient reaction rate.
- The reaction must be carried out at a low peptide concentration to prevent polycondensation.
- Piperidine (**11**) is a suitable base for the reaction.

10.6 (6 pt)

Draw the structures of intermediate **E** (including stereochemistry) and reagent **F**. Abbreviate intermediate **8** as **(vii)** and the protecting group as **PG-1** in structures **E** and **F** as depicted in **Scheme 5** in the question sheet.

E

F

10.7 (2 pt)

Determine the lowest possible molar equivalents of compound **12** that are necessary to enable full conversion of **8** to **13**.