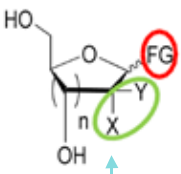
SPE
Summit Pharmaceuticals Europe

Phosphoramidites

Overview

Kolonhas been supplying **refined high-purity APIs and Intermediates** using our core technology, **Sugar Chemistry**. Our sugar chemistry consists of (1) control of functional groups (2) various refinement & crystallization methods (3) scale-up experience.

KLS Sugar / Nucleoside Chemistry



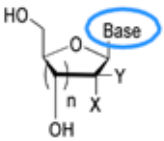
Functional group: OBz, OAc, Cl, Br, etc
2-deoxy anilide: 400Ton/year
MDR: 10Ton/year
2-deoxy ribose: 400Kg/year

X, Y: H,OH,alkyl,Amine, Cl, Br, F, etc

1. 2'-modification

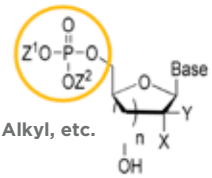
Monosaccharide derivatives
(Ribose, Glucose, Arabinose etc.)

2. Base modification



Base: Purine, Adenine, Cytosine, Uracil, Thymine, etc
Thymidine: 5Kg/Bx.
IPdR(New Drug): 8Kg/Bx

3. Phosphorylation



Z^1, Z^2 : H, OH, Alkyl, etc.

Phosphoramidate prodrug
Bucladesin: Lab Process

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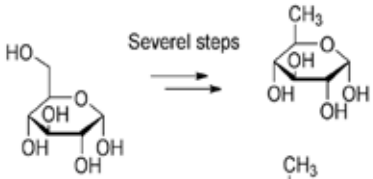
New Drug Intermediate / API

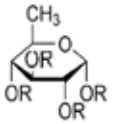
1. 2'-modification derivatives



Severel steps

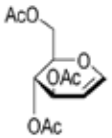
6-Deoxy-D-glucose (New drug intermediate) - 1Kg/Bx.

D-Glucose

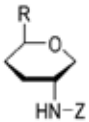


TEAD (New drug intermediate) - 5Kg/Bx.

R = OAc

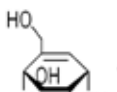


Severel steps

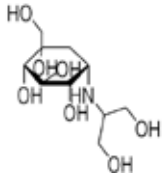


Triacetylglucal

New drug intermediates
BTPC - 35Kg/Bx
DPZ - 65Kg/Bx

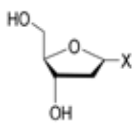


Valienamine



Voglibose (API) - 10Kg/Bx

2. Base modification



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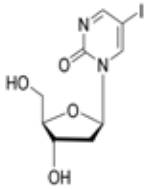
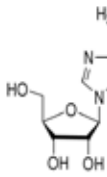
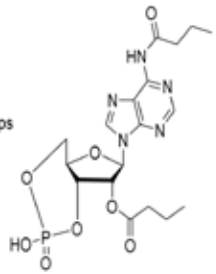


IPdR (New Drug): 8Kg/Bx

3. Phosphorylation



Severel steps



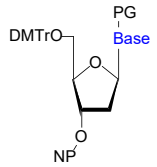
Adenosine

Bucladesin (API): Lab Process

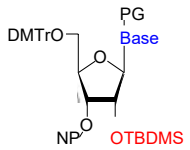
Product List

Kolonhas completedthe synthesis of **23 Phosphoramidites** through sugar/nucleoside chemistry. Each of them can incorporate flow chemistry, scale up, specific quality control and customization.

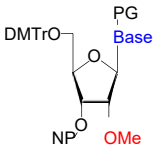
DNA Phosphoramidites



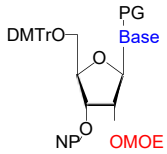
TBDMS-RNA Phosphoramidites



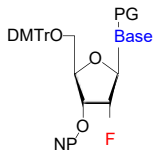
2'-Modified Phosphoramidites (2'-OMe)



2'-Modified Phosphoramidites (2'-O-MOE)



2'-Modified Phosphoramidites (2'-F)



Quality Control

Asthe basic qualitycontrol methods for Phosphoramidites, Kolon conducts **^{1}H NMR, ^{31}P NMR, UV, TLC,HPLC. LC/MS, GC/MS and MASS Spectrum** are used for stricter management of impurities that has adverse effects on Oligo synthesis.

- ^{1}NHMR
- ^{31}P NMR
- UV –The UV test provides 4 values of data
- TLC
- HPLC >98%
- LC/MS
- GC/MS
- ESI-MS

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Differentiation

- Securing product competitiveness through differentiated process development.
- Preoccupation of the market through early establishment of GMP process.

Stage 1. Fast Follower

- **Completion of general-purpose phosphoramidite development through competitor's product analysis**.
  - Continuously expanding the product portfolio with customer requests.

- **Promotion through collaboration with top 3 oligonucleotide makers around the world.**

Stage 2. Differentiation

- **Securing cost competitiveness through differentiated process development.**
  - Reducemanufacturing costs by developing switchable continuous manufacturing process suitable for small-scale multi-variety production.
  - Development of crystallization process to replace column process.

- **Diversification of Portfolio and development of customization.**
  - Development of a product linethatcan beusedtomanufacture oligonucleotides in the future (Diester, Triester, etc.).
  - Development of various product lines to meet customer needs (Back-bone modification, 5'-capping, etc.).

Stage 3. First Mover

- **Itis scheduled to build a production facility of 300 kg per year inthe Kilo-Lab Center in 2025.**
- **Aproduction base of 3 MT per year will be established inthe GMP plant in 2027.**
  - There isa highprobabilitythatregulationwillbestrengthened asthe RNA market grows.