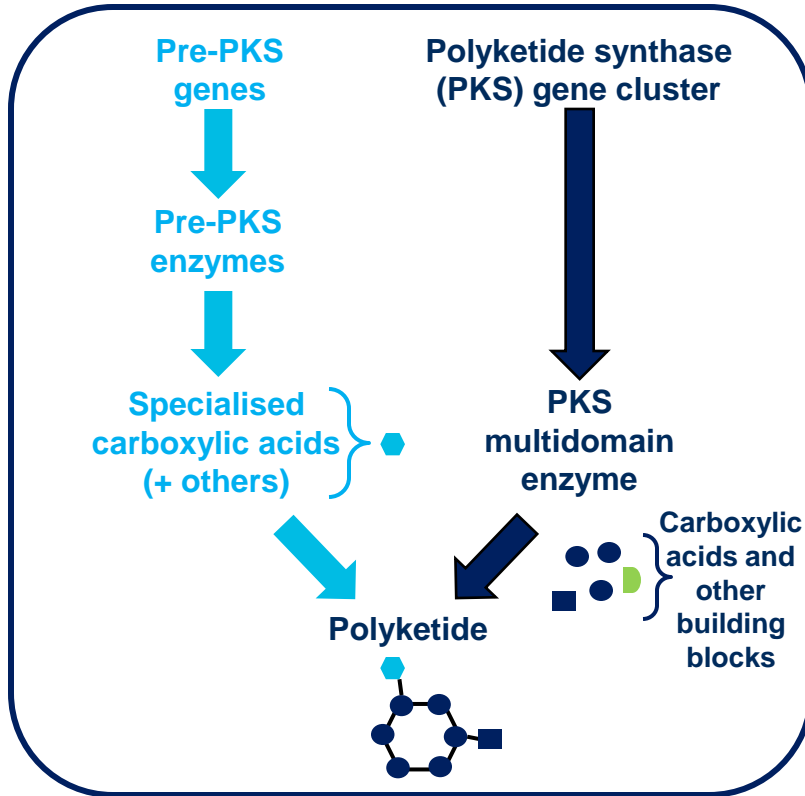


# Biotica's novoPT™ system

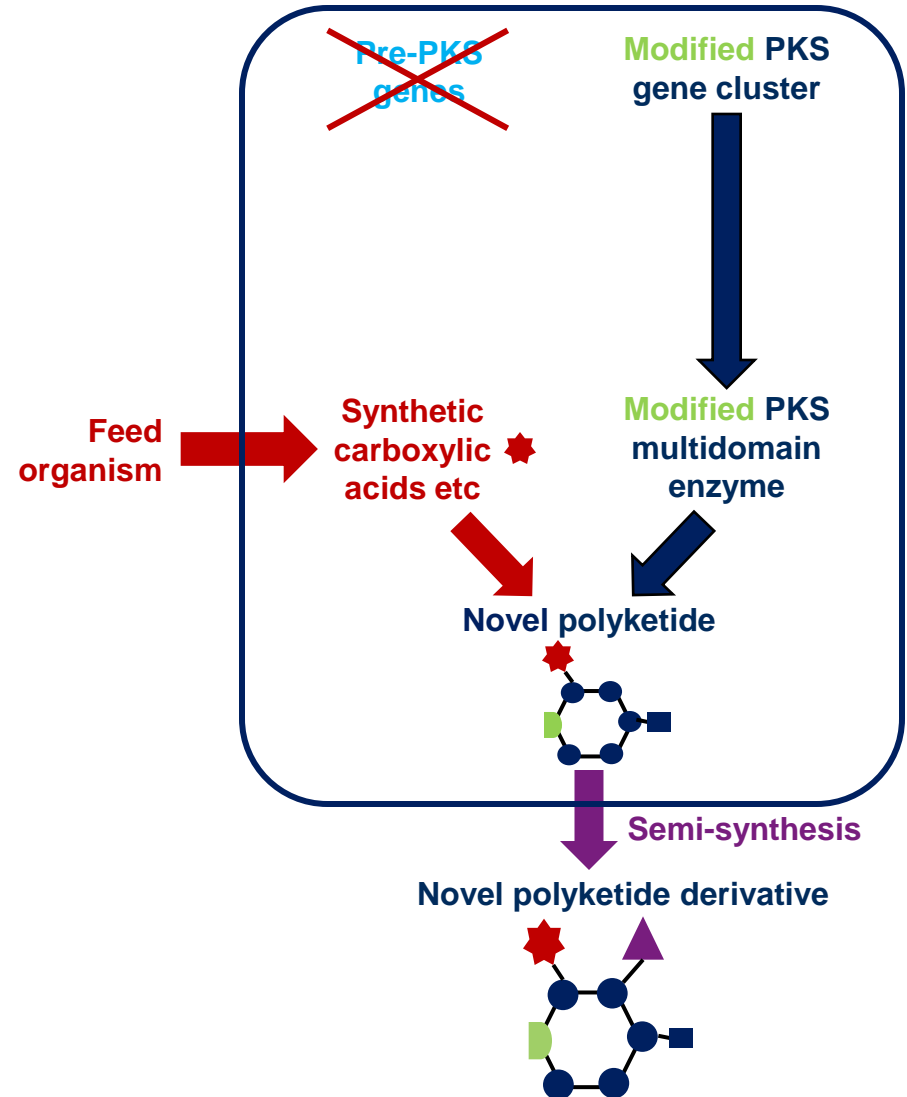
Creating commercial therapeutics from polyketide leads

# Overview of novoPT™ optimisation methods

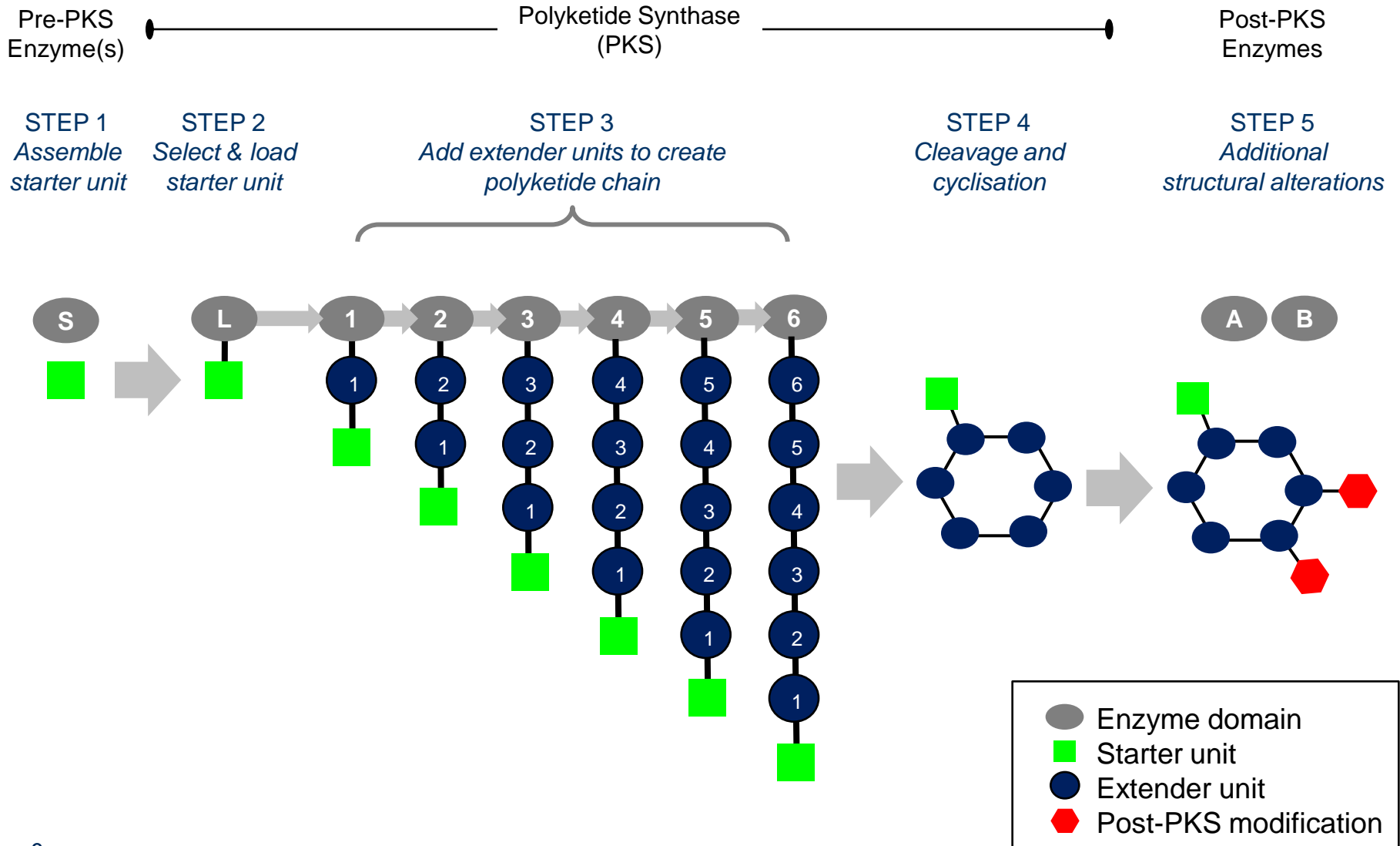
## Polyketide production in a normal cell



## novoPT™

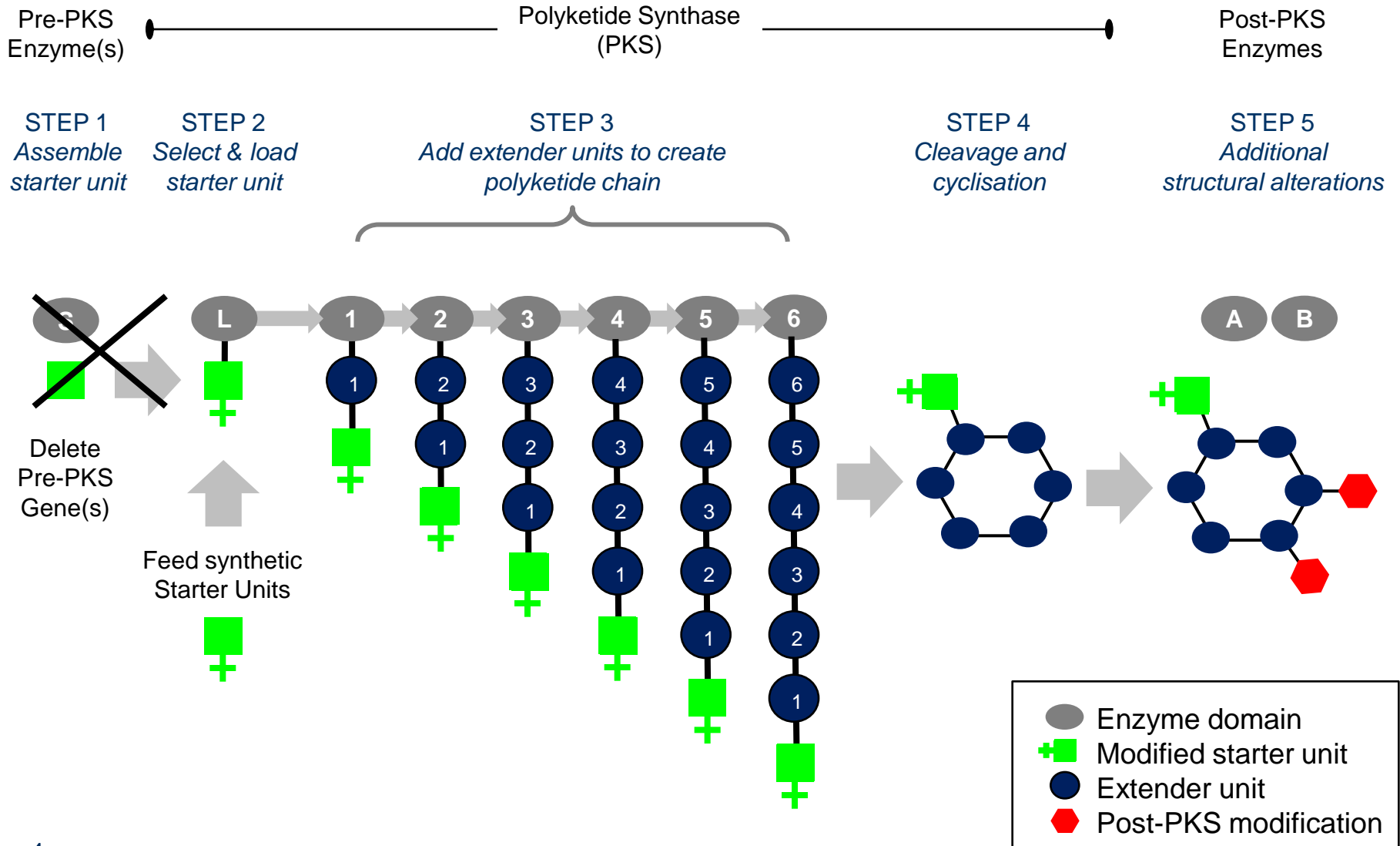


# Schematic structure and action of PKS enzyme cluster



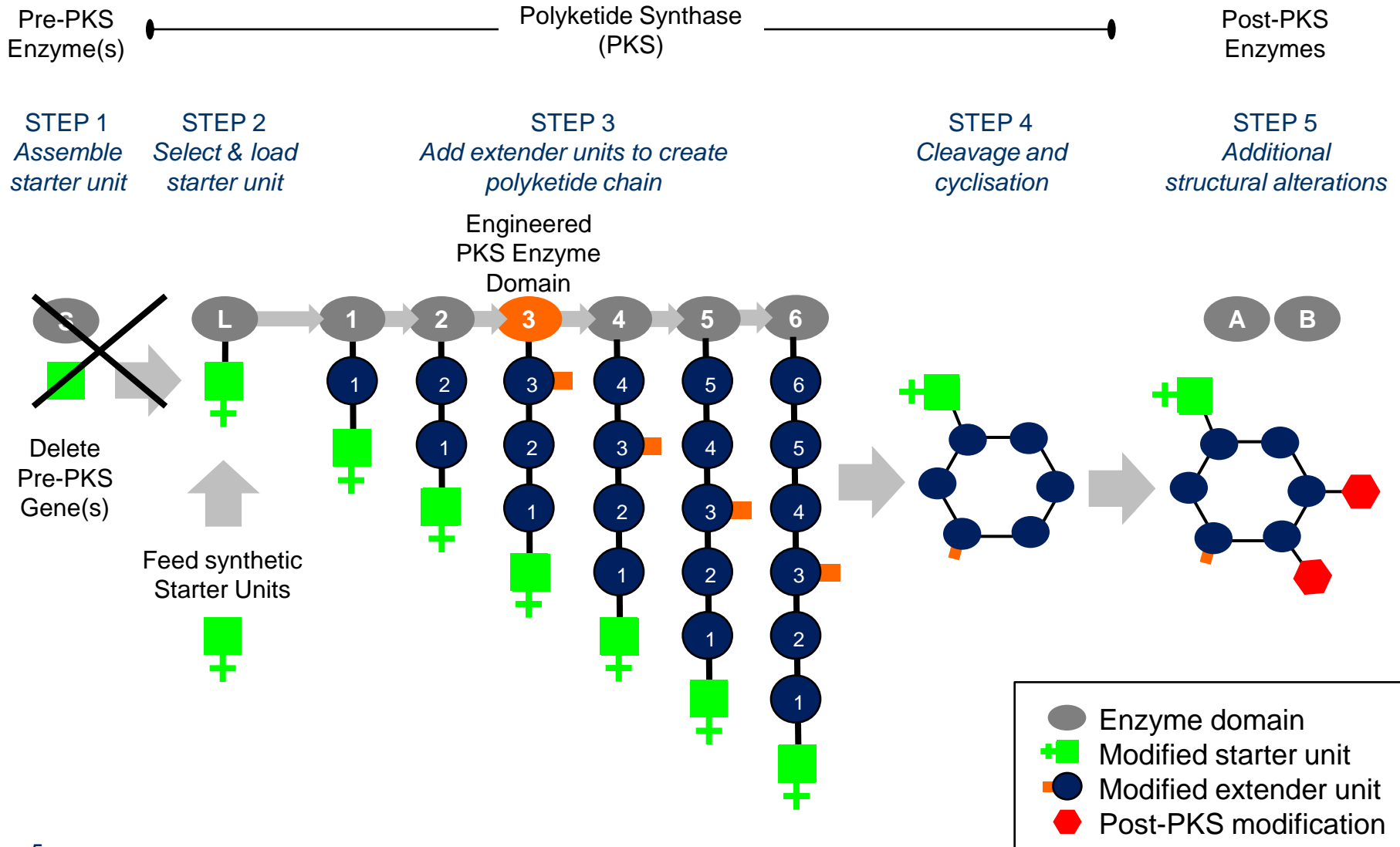
# Examples of bioengineering

## Method 1: mutasynthesis



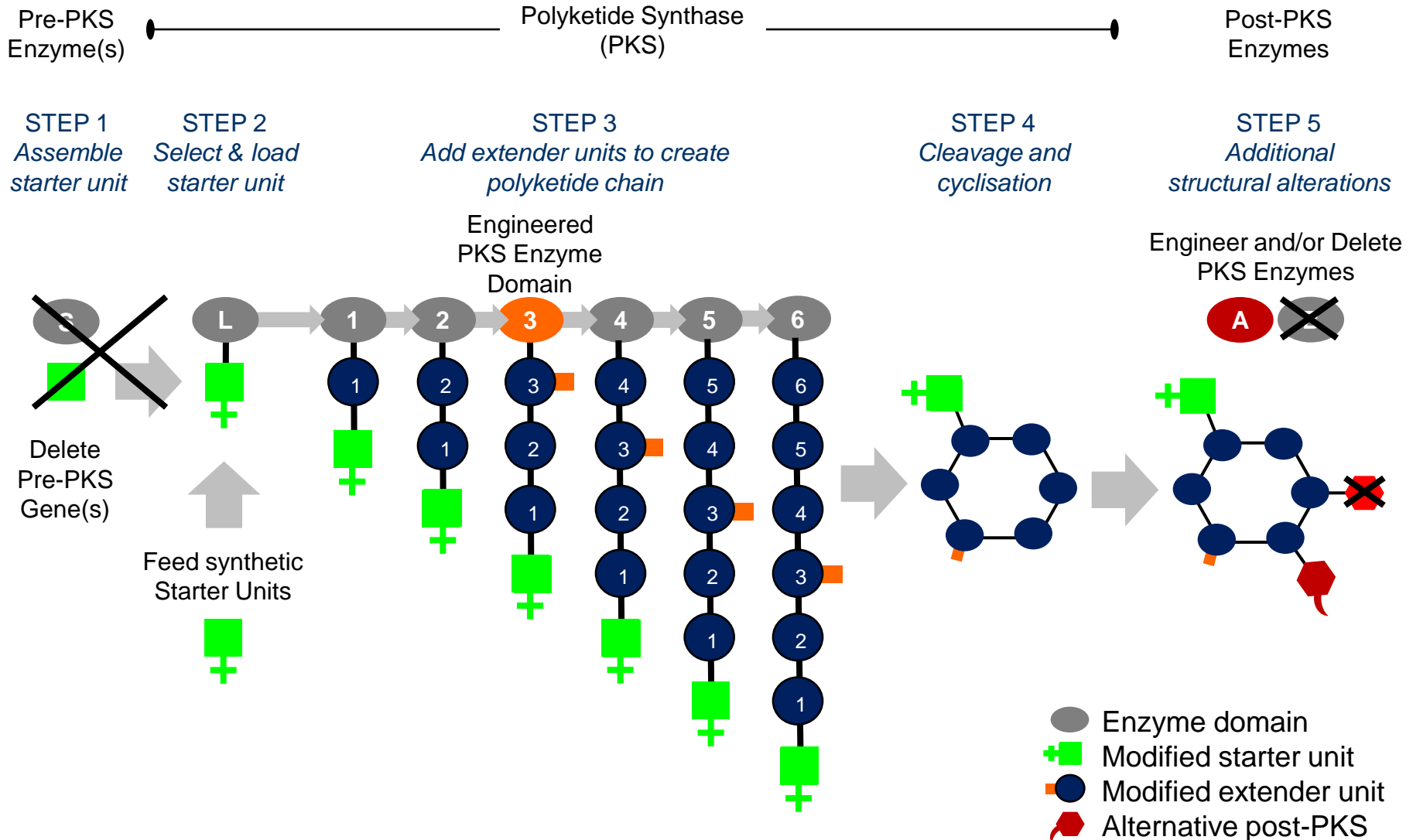
# Examples of bioengineering

## Method 2: PKS engineering



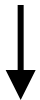
# Examples of bioengineering

## Method 3: Post-PKS Engineering



# Combining bioengineering methods: Rapamycin lead optimisation

Rapamycin

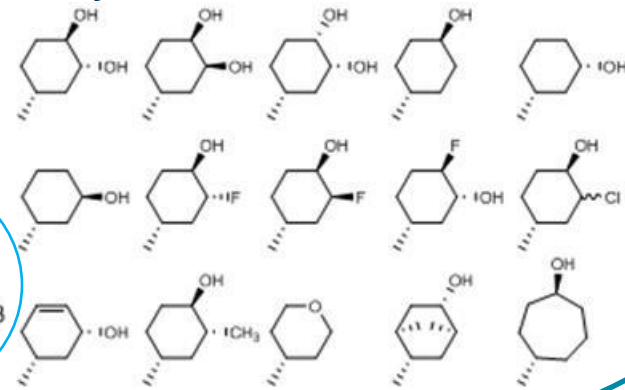


7 Engineering Themes

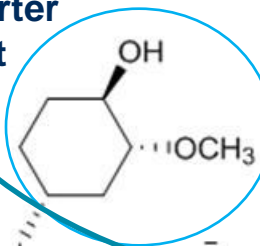


Combinatorial Library  
100+ Rapalogs

## Mutasynthesis Synthetic starter units



Starter unit



Changes made by  
PKS and Post-PKS  
Engineering

H,OH

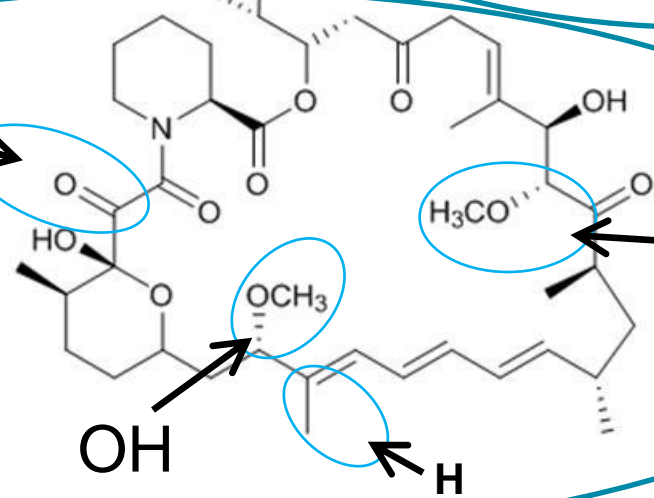


H<sub>3</sub>CO

H,OH

OH

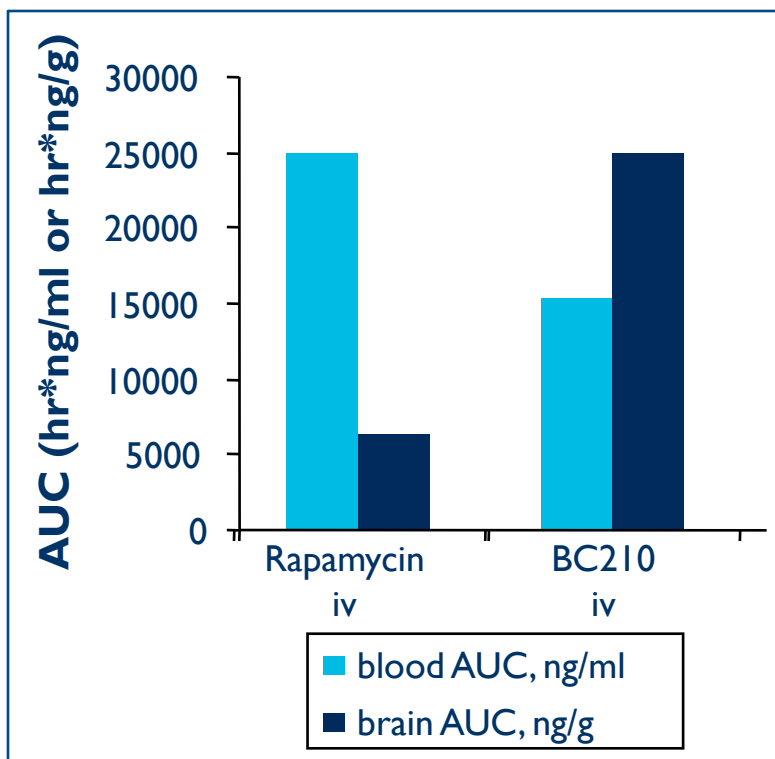
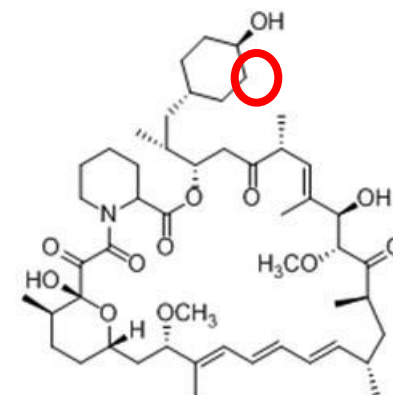
H



# Example: rapalog BC210 engineered for improved PK

## BC210:

- Major metabolism site removed through mutasynthesis
- PK properties improved
- Crosses blood-brain barrier



	Rapamycin	BC210
<b>Murine <math>t_{1/2}</math> (min)</b>	<b>40</b>	<b>59</b>
<b>Caco-2 <math>P_{app}</math> (nm/s)</b>	<b>2</b>	<b>29</b>
<b>Caco-2 B-A/A-B</b>	<b>458</b>	<b>15</b>

# Summary of novoPT™ polyketide lead optimisation

## **novoPT™ polyketide lead optimisation:**

- Starting point is biology-rich natural polyketide active against chosen target
- Rational modification through engineering the polyketide synthase (PKS) and semi-synthesis
- Combine multiple methods to generate targeted compound libraries

## **Therapeutic benefits of novoPT™ polyketide therapeutics:**

- High-content chemistry of polyketides gives access to difficult drug targets
- Characteristics tailored for pharmaceutical use by **novoPT™**
- Address diseases of high unmet need not well treated by other methods

## **Commercial benefits of novoPT™ polyketide therapeutics:**

- Novel, patent protected compounds inaccessible to traditional medicinal chemistry
- Additional layers of protection through Biotica know-how and patents on optimisation methods
- Strain development for commercial production further enhances exclusivity