

BIO LIMUS A9™

Designed for vascular stent technologies

The drug designed
for vascular stent technologies



BIOSENSORS
INTERNATIONAL™

BA9™: Second Generation Limus Drug

Dedication to excellence

Biosensors started to manufacture drug-eluting stents (DES) in the early 2000's. Whilst some mTOR inhibitor limus drugs were available for systemic applications, Biosensors' belief was that these drugs had not been specifically developed for stent application.

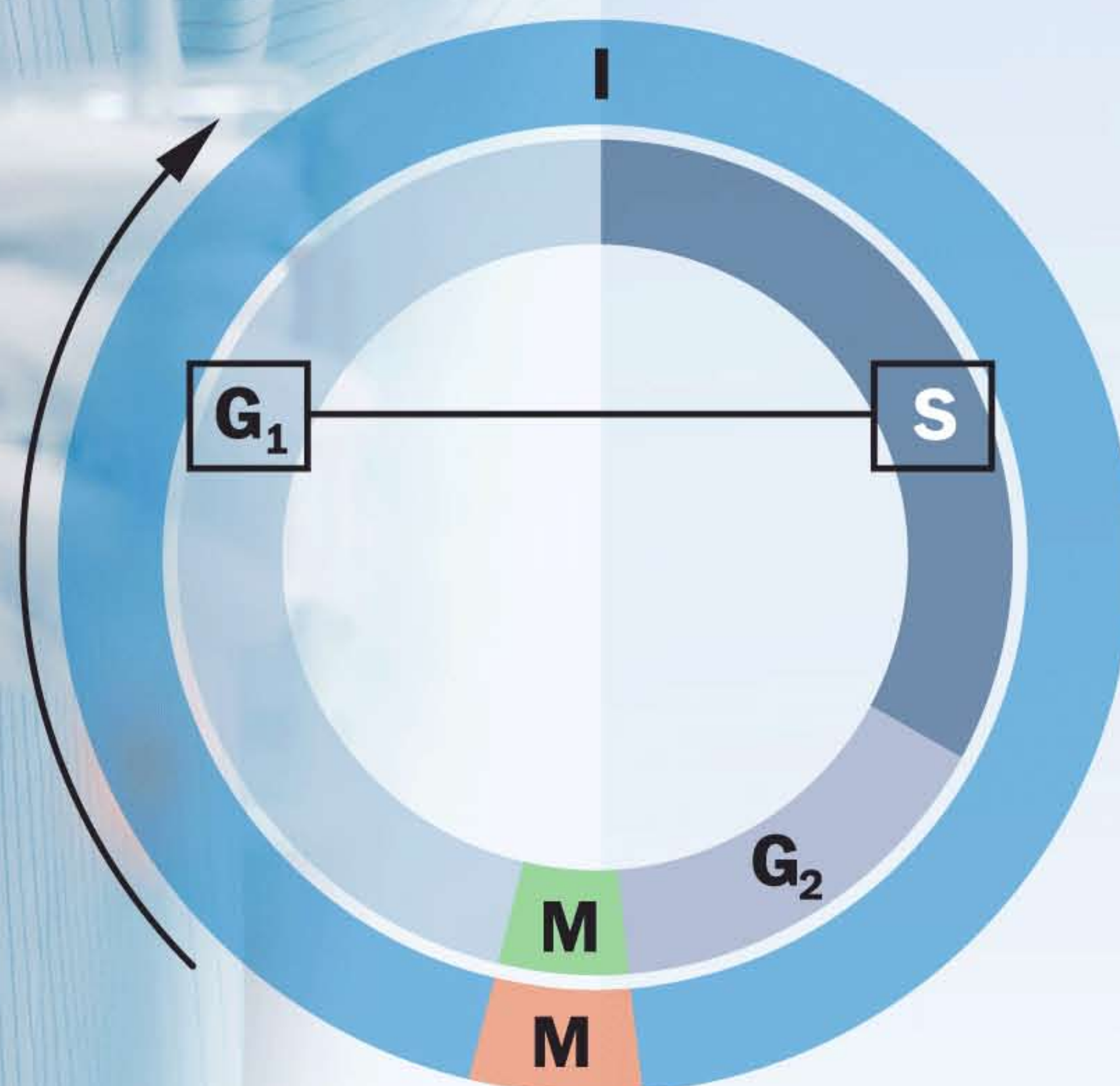
By focusing during the early stages of drug development on its use for vascular technologies, Biosensors believed that improvements could be made.

The R&D team started with the development of Biolimus A1 and, through a number of iterations, ultimately decided to focus on BA9 (Biolimus A9), which was evaluated as the best option for the coronary stent application.

Biosensors' proprietary BA9 drug was designed for our vascular stent technologies and is found on the BioMatrix™ family of DES and BioFreedom DCS

BA9 inhibits cellular proliferation:

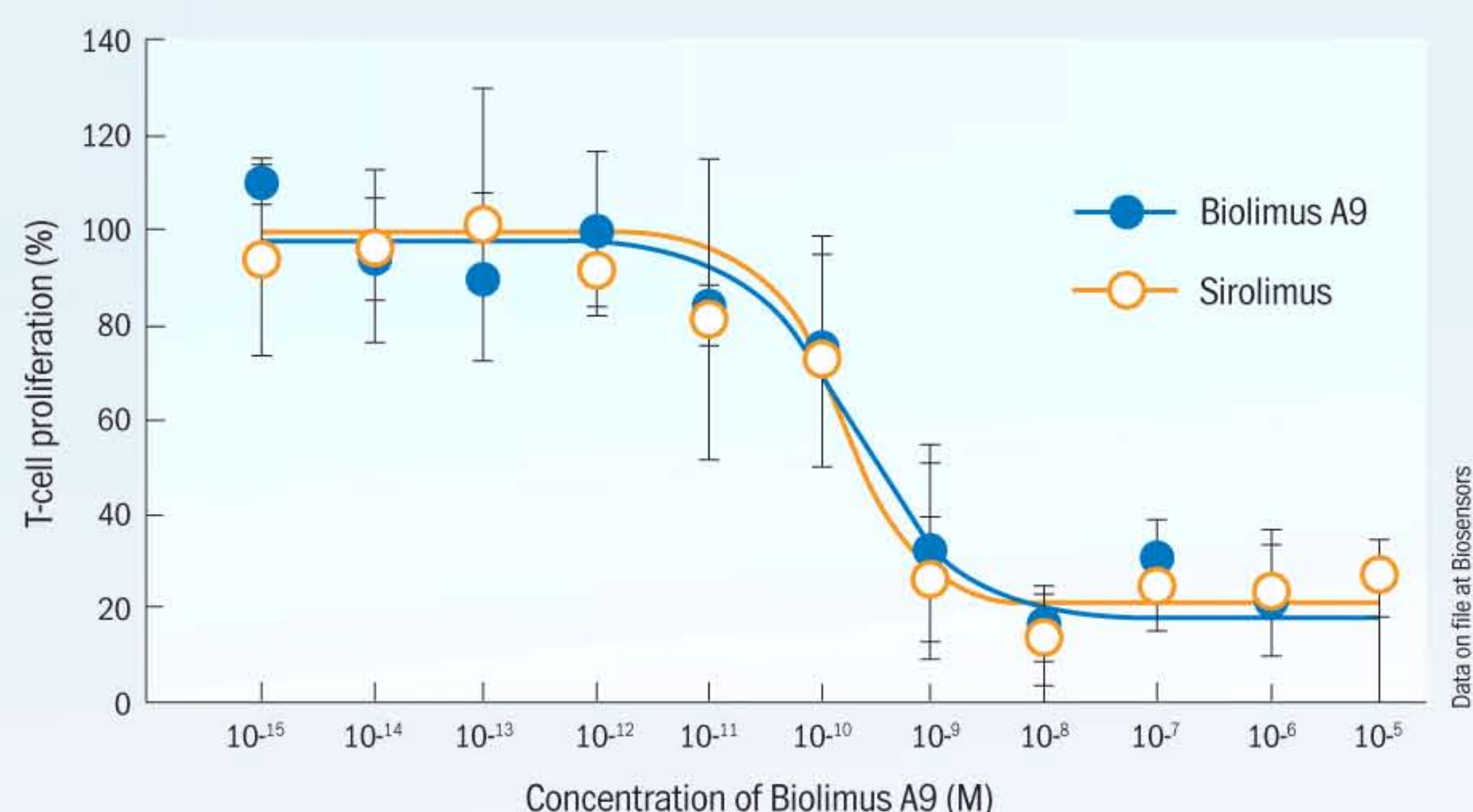
mTOR inhibitors such as **BA9**, Sirolimus, Everolimus and Zotarolimus inhibit cellular proliferation. i.e. prevent the transition from G₁ to S phase



Cell cycle schematic

Same mechanism of action and metabolic pathway

Mechanism of action

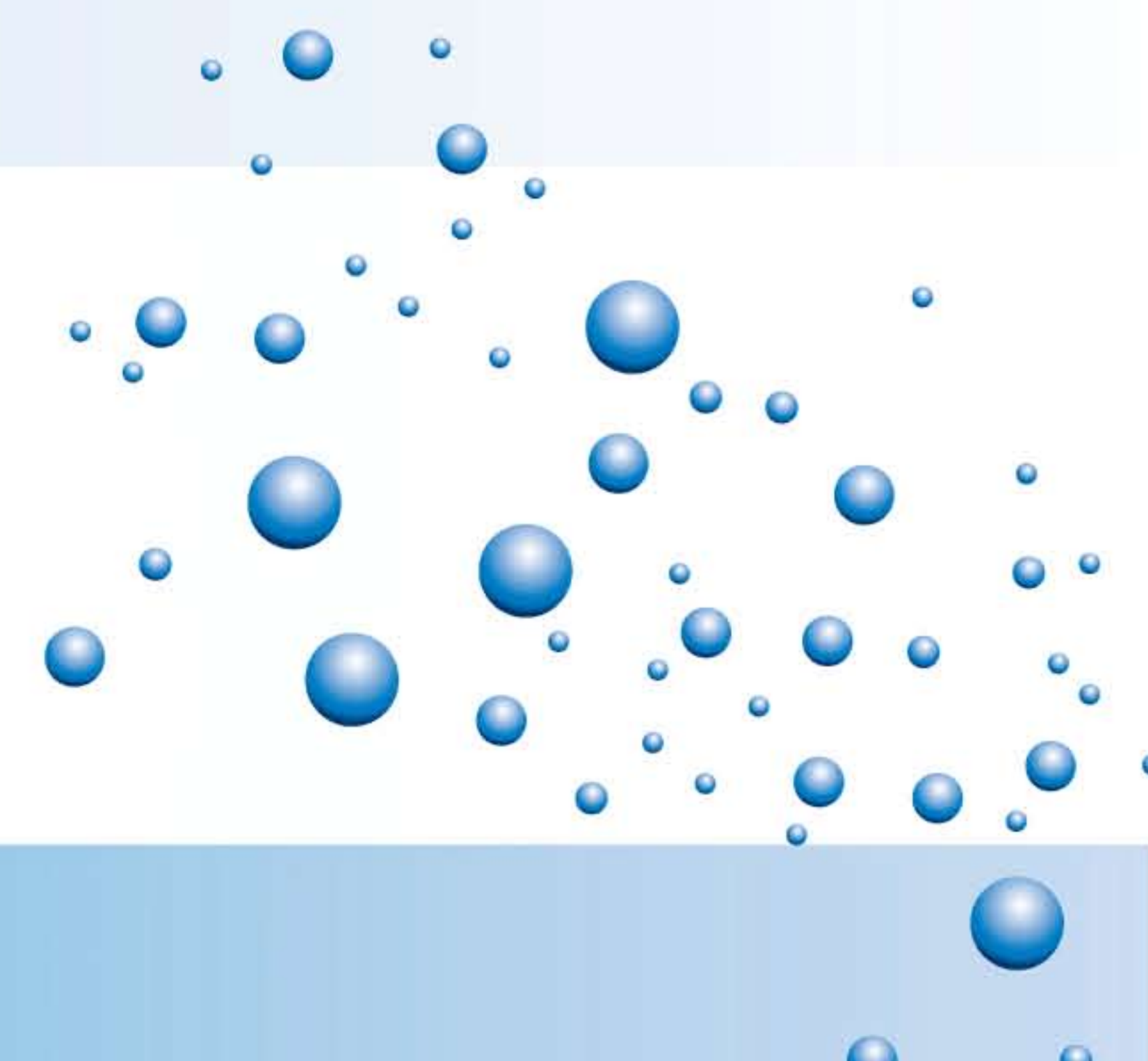
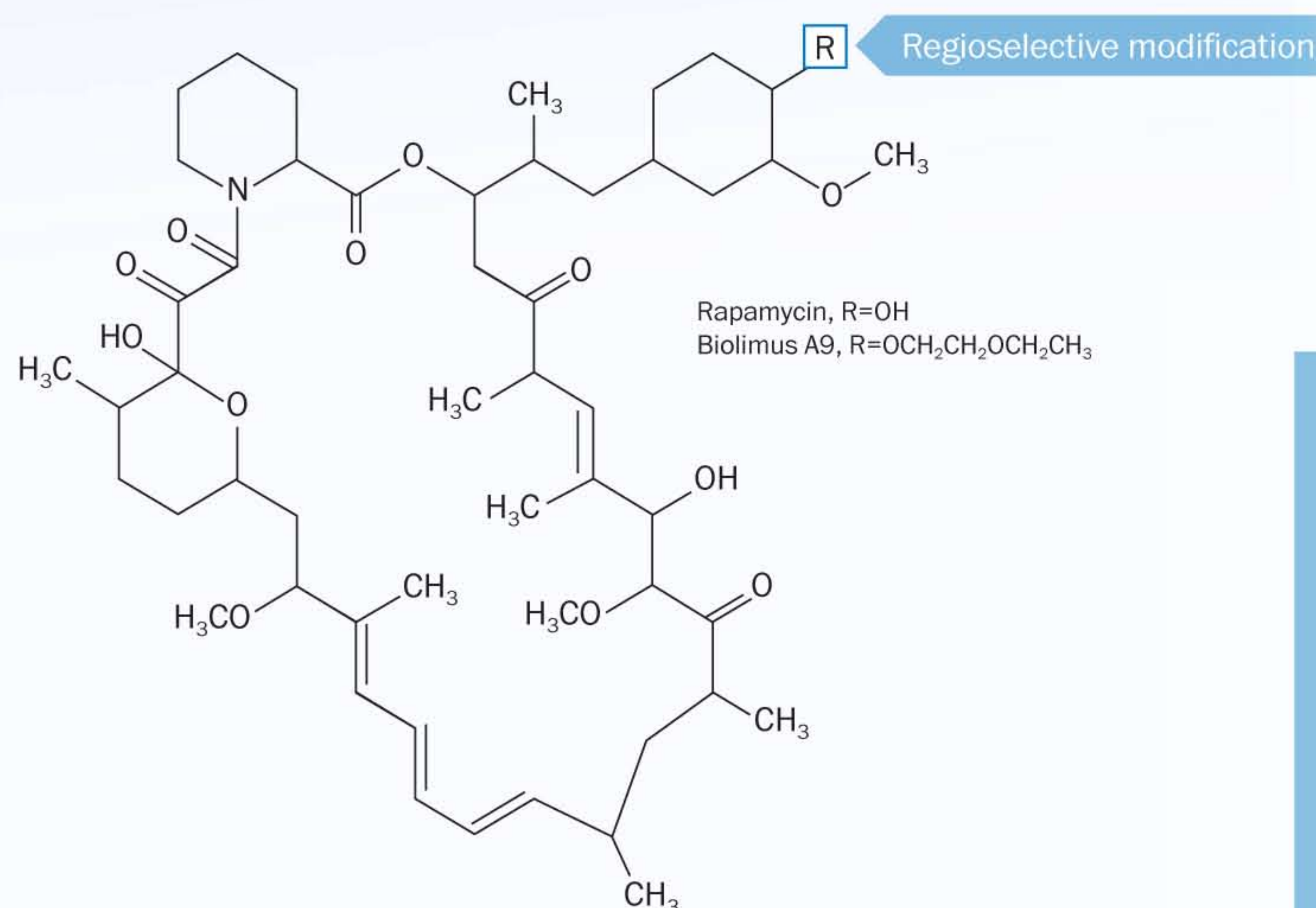


Inhibitory effect on human T-lymphocytes and vascular smooth muscle cells is similar for BA9 and sirolimus

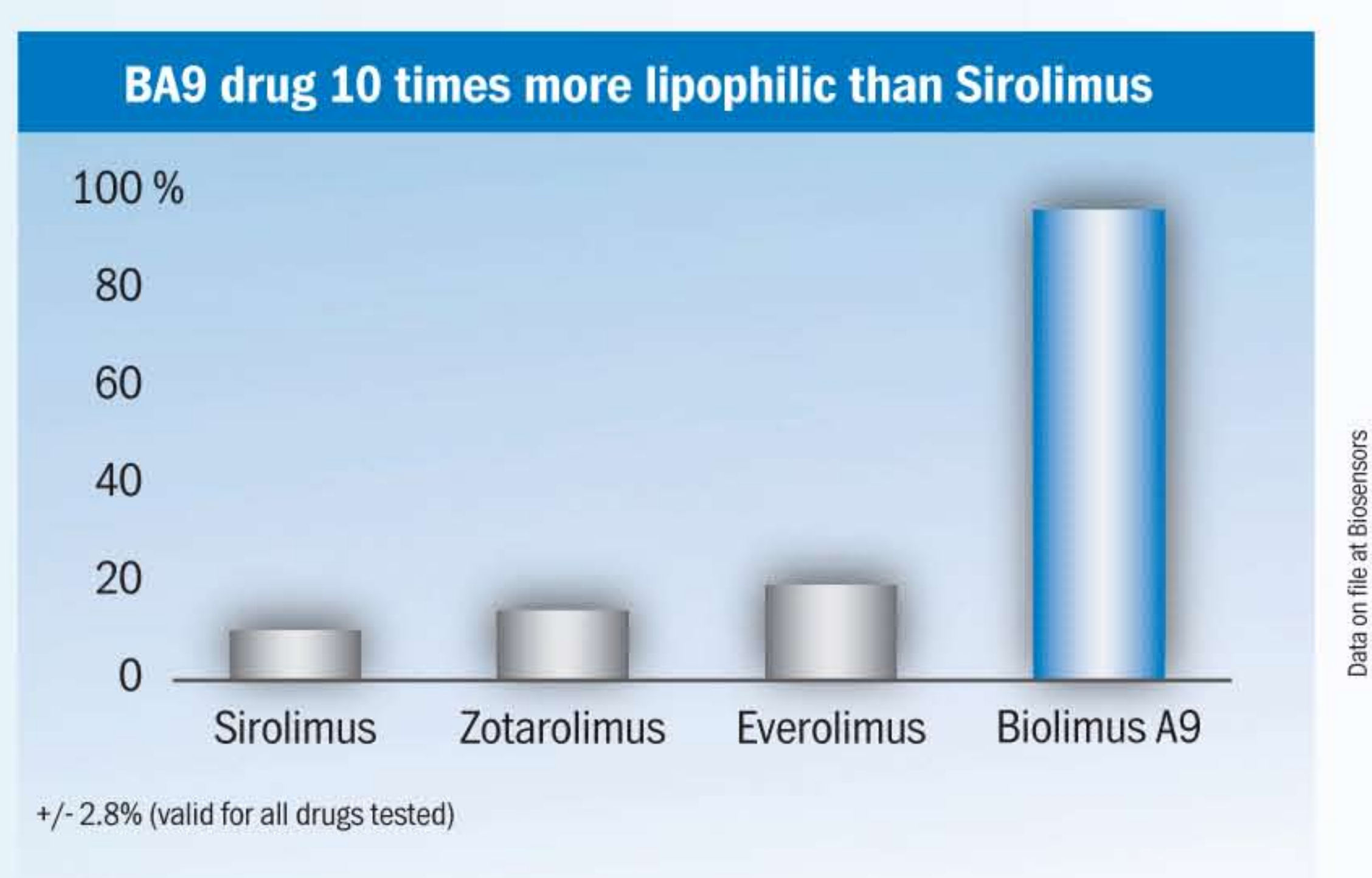
Similar to sirolimus and everolimus, the highest metabolic activity of C14-BA9 was seen with CYP3A4

- > Based on same overall macrolide structure as mTOR inhibitors sirolimus and everolimus
- > Difference in lipophilicity attributed to regioselective modification at position R
- > High local bioavailability* compared with other similar mTOR inhibitors

* Bioavailability here refers to the amount of whole drug molecules that are available to act on the treatment area



BA9: Lipophilic by design



BA9 is designed for targeted local applications such as with drug eluting or drug-coated stents

- ✓ **Same mechanism of action**
BA9 structure retains the sirolimus macrolide ring structure
- ✓ **BA9 is more lipophilic**
due to regioselective modification
- ✓ **BA9 structure slows metabolism of drug** by changing the affinity for enzymatic elimination
- ✓ **BA9 greater local bioavailability**
- ✓ **BA9 local tissue warehousing** allows for sustained local drug release without polymer and with minimal systemic exposure



BIOLIMUS A9™

Designed for vascular stent technologies



**Developed by Biosensors
to treat vascular disease using stent technologies...**

- > The inherent properties of BA9 differentiate it from the other common mTOR inhibitor limus drugs
- > BA9 is more lipophilic due to regioselective modification for more targeted effect
- > BA9 has greater local bioavailability than Sirolimus and Everolimus
- > BA9 structure slows drug metabolism by changing the affinity for enzymatic elimination
- > BA9's improved local tissue warehousing, provide Biosensors with a unique proprietary drug that is a key component of the BioFreedom DCS

Data on file at Biosensors International for any sustained claims in this brochure.

Biolimus A9 and BA9 are trademarks or registered trademarks of Biosensors International Group, Ltd.
All cited trademarks are the property of their respective owners.

Not available for sale in the United States and certain other countries.
© 2015 Biosensors International Group, Ltd. All rights reserved.

www.biosensors.com

 **BIOSENSORS**
INTERNATIONAL™

BIOSENSORS EUROPE SA
Rue de Lausanne 29
1110 Morges
Switzerland
Tel: +41 (0)21 804 80 00
Fax: +41 (0)21 804 80 01

**BIOSENSORS INTERVENTIONAL
TECHNOLOGIES PTE LTD**
36 Jalan Tukang
Singapore 619266
Tel: +65 6213 5777
Fax: +65 6213 5737