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**MICRO LABS LIMITED AND  
MICRO LABS USA INC., Petitioner,  
v.  
SANTEN PHARMACEUTICAL CO., LTD. AND  
ASAHI GLASS CO., LTD., Patent Owner.**

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Patent Owner's Demonstratives  
September 6, 2018

Case IPR2017-01434

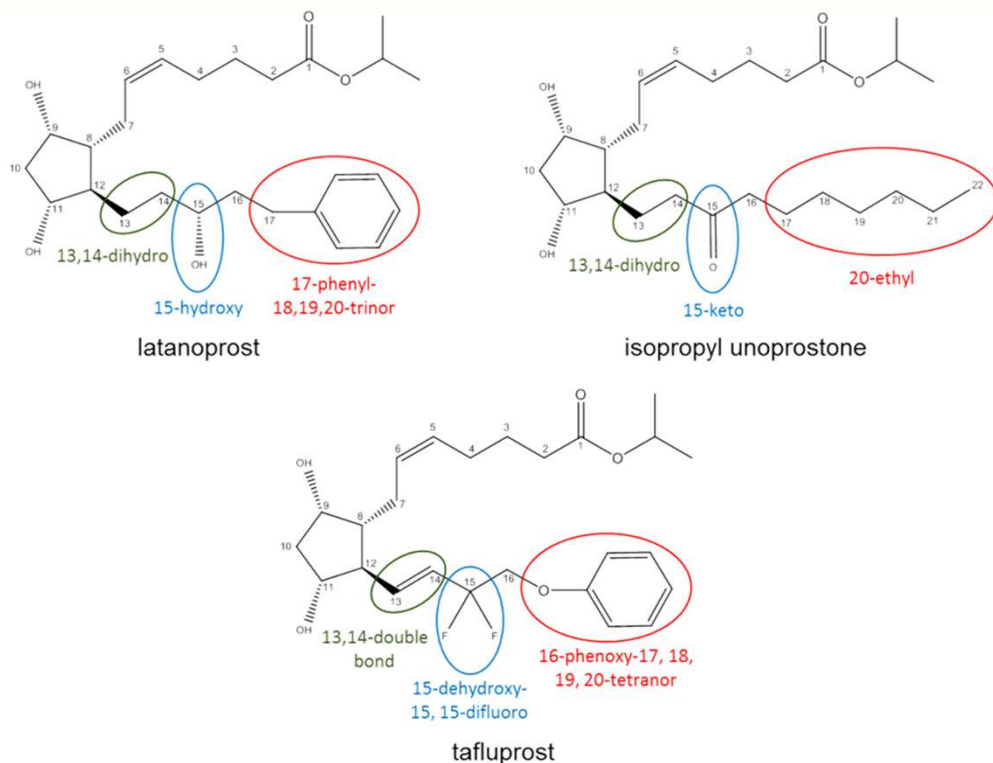
Patent No. 5,886,035

**Santen AGC**

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## Tafluprost Differs from 2 Commercially Available PG Analogs in 3 Ways



- Only tafluprost has **2 Fs** at 15 position (v. OH)
- Only tafluprost has **phenoxy** at 16 position

# Medicinal Chemistry of Prostaglandins Highly Unpredictable

- Medicinal chemistry of prostaglandins highly unpredictable as of December 1996 (and remains so today)

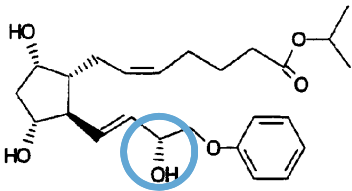
As is apparent in Table 2, the five compounds differ only slightly in structure; however, as Examples 5 and 6 will show, such seemingly slight structural differences produce greatly different IOP-lowering effects and levels of hyperemia.

	COMPOUND NAME	COMPOUND STRUCTURE
A	Cloprostenol, isopropyl ester	
B	Fluprostenol, isopropyl ester	
C	16-Phenoxy-17,18,19,20-tetranor PGF <sub>2α</sub> , isopropyl ester	
D	17-Phenyl-18,19,20-trinor PGF <sub>2α</sub> , isopropyl ester	
E	13,14-Dihydro-17-phenyl-18,19,20-trinor PGF <sub>2α</sub> , isopropyl ester	

Ex. 1003 (Klimko), 15:54

Ex. 1003 (Klimko), 15:1-50 (Tab

## Petitioner's Proposed Trajectory from Compound C to Tafluprost Made in Hindsight

Proposed Scheme	Asserted Prior Art	
<p>Compound C as lead compound</p> <div data-bbox="180 1031 1031 1308" style="border: 1px solid black; padding: 5px;"> <p><b>C</b>   16-Phenoxy-17,18,19,20-tetranor PGF<sub>2α</sub> isopropyl ester</p>  <p>Ex. 1003 (Klimko), 15:1-50 (Table 2)</p> </div>	<ul style="list-style-type: none"> <li>• Klimko (Ex. 1003)</li> </ul>	<ul style="list-style-type: none"> <li>• Not a Com</li> <li>• Other Supe</li> <li>• Intol (Hyp</li> <li>• Unfa (Initi</li> <li>• No " Effic</li> </ul>
<p>Replace 15-OH with 15-H to diminish side effects</p>	<ul style="list-style-type: none"> <li>• Kishi (Ex. 1004)</li> </ul>	<ul style="list-style-type: none"> <li>• Char Redu Activ</li> </ul>
<p>Replace 15-H with 15-F to mimic (removed) 15-OH</p>	<ul style="list-style-type: none"> <li>• Bezuglov 1982 (Ex. 1007)</li> <li>• Bezuglov 1986 (Ex. 1008)</li> <li>• Ueno Japan (Ex. 1006)</li> </ul>	<ul style="list-style-type: none"> <li>• Char Hope IOP- But M Side</li> </ul>
<p>Inserting 2Fs at C15</p>	<ul style="list-style-type: none"> <li>• Ueno Japan (Ex. 1006)</li> </ul>	<ul style="list-style-type: none"> <li>• 2Fs ≠</li> </ul>

## Petitioner Picked Compound C as Lead Based on I

- The standard:

Importantly, "[a]bsent a reason or motivation based on such prior art evidence, mere structural similarity between a prior art compound and the claimed compound does not inform the lead compound selection." *Id.* "Were it otherwise, the analysis would impermissibly rely upon *ex post* reasoning. *Id.*

Paper 22 (POR), 27-28 (citing *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1292 (Fed. Cir. 2012))

- But Petitioner's expert, Dr. deLong, worked backwards from tafluprost to get to Compound C:

A. Okay. In the issue at hand with tafluprost, one of the three compounds in one of the claims is a chloride in there. So had the -- had the company taken the chloro one as one of those three instead of the nonchloro one, we would say, "Well, it's more appropriate to have the chloro one be the lead compound because that's the closest one to the chloro tafluprost in -- in that claim in -- in their patent.

Ex.2025 (79:13-22

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