

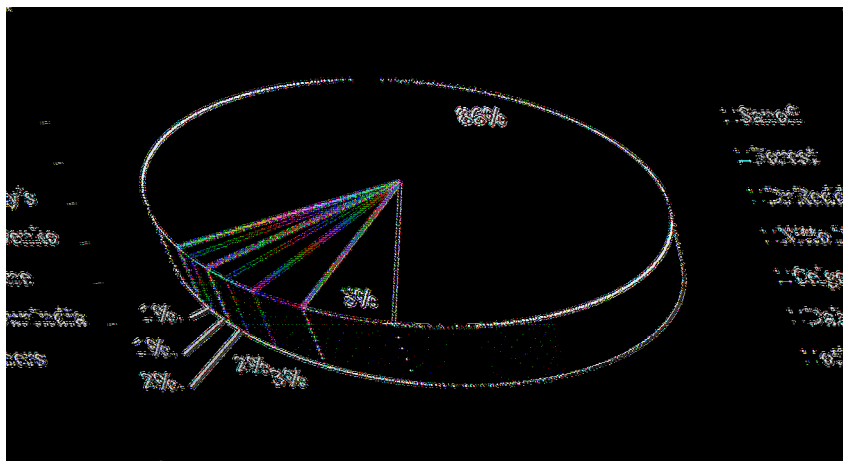
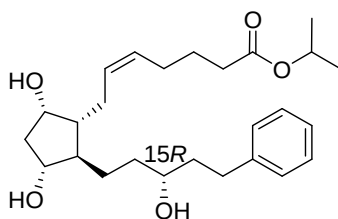


Figure 3: Top patent applicants for docetaxel (474 patents)<sup>74</sup>

### B. Xalatan

## 1. General

Latanoprost (trade name Xalatan: Formula 3) is an ophthalmic solution used to treat glaucoma and ocular hypertension by reducing elevated intraocular pressure.



### Formula 3

74 *Id.*

The compound has been originally disclosed in EP 0364417 B1<sup>75</sup> belonging to Kabi-Pharmacia. The drug was launched in 1996 in the U.S. and in Europe<sup>76</sup>. The patent protection for the basic compound expired in March 2011.

During previous research at Columbia University<sup>77</sup> it had been found that prostaglandine PGF<sub>2α</sub> and its iso-propyl ester could lower the intraocular pressure in patients with open-angle glaucoma. However, these compounds had low therapeutic value due to the poor cornea permeability and their side effects (e.g. ocular irritation, conjunctival hyperemia). Further studies at Kabi Pharmacia addressed these issues. Variation in the structure of PGF<sub>2α</sub> allowed achieving the desired effects. Furthermore, a more efficacious compound was obtained by separating the 15*R*-epimer (Formula 3). The ester prodrug is hydrolyzed on the cornea and the parent acid is active as a selective prostaglandin F-receptor agonist and reduces the intraocular pressure preventing further optic nerve damage and preserving remaining vision.<sup>78</sup>

## 2. Patent Portfolio

### a) Process

The initial method of synthesis covered by the basic patent family (EP 0569046 resp. WO 90/02553) was based on the final separation of the two epimers at C15 (Formula 3) resulting therefore in a tedious procedure and in low yield taking in account the fact that only the 15*R*-epimer is desired. Further studies were therefore directed to solve the

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75 Filed in September 1989 and invoking a Swedish application priority: SE 8803110 and SE 8803855.

76 E.g. Marketing Authorisation in Sweden 18 July 1996: see European Patent Register, Legal status: EP 0364417, <https://register.epo.org/espacenet/application?number=EP89850294&lng=en&tab=legal>, (last visited Aug. 3, 2012).

77 U.S. 4,599,353.

78 Information about Xalatan were taken from Sajiv K. Nair, Kevin E. Henegar, *Modern Drug Synthesis* 329-330 (Jie Jack Li, Douglas S. Johnson eds., 1st ed. 2010).