

## **The first technology for immediate, bioregulated release of diclofenac in new pharmaceutical forms**

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**This system enabled APR to develop improved conventional oral forms (e.g. 25 and 50 mg diclofenac sodium or potassium tablets) as well as to develop and validate new oral fast acting pharmaceutical forms never marketed before with this active ingredient (Drops at 5% and 25 and 50 mg of diclofenac potassium Sachets).**

The surely most innovative APR's formulation is the diclofenac potassium drops at 5% which is the first, fast acting (C<sub>max</sub> in 13,68 min), completely palatable and free from aftertaste diclofenac potassium formulation available, perfectly stable at ICH conditions, showing a consistent regular absorption associated with a reduction of gastric side effects. In addition, drop formulations enable to improve flexibility in the posological scheme. APR's drop formulation has been already tested in several administration conditions such as cold/hot water, fruit juice, hot tea, etc. Supported by preliminary very successful in vitro and in vivo results, APR is about to start full clinical development of the drop formulation of pure diclofenac potassium at 5% for which there are several on going negotiations for licensing out in Europe as well as in the US.

The 50 mg diclofenac potassium sachets has been already licensed out to Novartis Pharma for Italy on an exclusive basis where the product has been already registered on March 99 by the local MOH and the launch is expected by February 2000; the economical terms of the agreement remain undisclosed. The product is mainly indicated as short term treatment of acute painful and inflammatory conditions such as sprains and strains, bruises, back pain, post operative pain, period pain, etc.

The 25 and 50 mg Diclofenac Potassium fast acting tablets have been already licensed out to a leading Swiss Company for Switzerland plus other East European Countries on an exclusive basis and the related registration file is expected to be filed in Switzerland by II Quarter 2000; on this agreement APR will receive undisclosed milestone payments according to the development steps.

APR applied for a patent protection worldwide (all the PCT Countries plus additional countries outside PCT) claiming this new technology and related patents were already granted in Italy and South Africa and it is still pending in all the other countries. Anyway APR has already carried out, through its Patent Attorney, a full patent validity search report supporting the technology. All the APR's formulations showed great advantages over reference drugs (Cataflam® and Voltaren® - Potassium Salt and Sodium Salt of Diclofenac respectively) in terms of rate of absorption and regularity of absorption. All the pharmaceutical forms developed by APR have demonstrated considerably higher peak plasma levels in a shorter period of time as well as a great reduction in the variability leading to very consistent profiles and reduced standard deviation among subjects as well as a strong reduction of the related gastric side effects.

All the APR's formulations have been technically up scaled and tested in a fully GMP approved facility in The Netherlands using worldwide accepted, non patent infringing process and formula enabling APR's licensees to successfully promote these innovative formulations even at the same prices of the generic market.