



PRESS RELEASE DRAFT CTRS / APHP  
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## Orphacol®: a collaboration between the AP-HP and the company Laboratoires CTRS on the treatment of rare liver diseases earns a high rating for clinical benefit from the French health authorities

The orphan drug Orphacol® (promoted by the pharmaceutical company Laboratoires CTRS) received the highest rating for improvement in actual benefit (<sup>1</sup>*Amélioration du Service Médical Rendu*, ASMR 1) from the French National Authority for Health's Transparency Commission. Orphacol® is the only treatment for inborn errors in primary bile acid synthesis - diseases that are extremely rare and usually fatal if not treated. Orphacol® enables patients with these diseases to avoid liver transplantation - an operation with very serious potential consequences, especially in young children.

**Orphacol® is an exemplary development of innovation and research at the Assistance Publique-Hôpitaux de Paris (AP-HP, the Paris Public Hospitals Group)** and is the first ASMR-1-rated drug to have come out of the AP-HP's academic research effort. This achievement marks the success of an exemplary, long-standing, public-private collaboration between the AP-HP's researchers, its General Agency for Equipment and Health Products (*Agence Générale des Equipements et Produits de Santé*, AGEPS), its Office for Technology Transfer and Industrial Partnerships (OTT & PI) and the company Laboratoires CTRS. The development of Orphacol® resulted from medical, pharmaceutical and industrial progress and exemplary relationships between the collaborating teams. The successful development of Orphacol® also demonstrates that although challenging, it is possible to produce drugs for a very small patient populations. This success opens us new possibilities for developing other orphan drugs. Hospital-based innovation and research by physicians and pharmacists has enabled the creation of innovative products and businesses, for the ultimate benefit of patients.

### **The development of Orphacol®**

In the early 1990s, Professor Emmanuel Jacquemin (from the Pediatric Hepatology and Liver Transplantation Unit at Bicêtre Hospital, part of the AP-HP's Paris South University Hospital) demonstrated that daily oral administration of cholic acid (Orphacol®'s active ingredient) could treat

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[1] Actual benefit (*Service Médical Rendu*, SMR) is a French standard that takes several medical parameters into account: the severity of the condition for which the drug is indicated and the performance of a particular drug in a given indication. An improvement in actual benefit (*Amélioration du Service Médical Rendu*, ASMR) refers to the contribution of a novel treatment relative to existing treatments. There are five ASMR ratings, of which ASMR 1 is the highest. The ASMR rating influences a drug's eligibility for reimbursement by the French public health insurance scheme and the reimbursement level.

young patients with extremely rare and serious hereditary diseases. Inborn errors in primary bile acid synthesis are due to a deficiency in either 3 $\beta$ -hydroxy-C27-steroid dehydrogenase/isomerase or  $\Delta^4$ -3 oxosteroid 5 $\beta$  reductase, leading to the accumulation of hepatotoxic metabolites and progression to irreversible cholestasis and liver failure (which are almost always lethal in the absence of treatment). Prior to this discovery, the only treatment for these inborn errors was liver transplantation, with all its associated consequences – especially since this operation generally had to be performed in the first few months or first years of life.

The initial results were particularly impressive and the Bicêtre Hospital's pharmacy produced the first capsules. Faced with sustained, increasing demand, the hospital contacted the AGEPS and the AP-HP's Pharmaceutical Laboratory with a view to taking over production of this hospital drug preparation. In 2002, the Pharmaceutical Laboratory obtained orphan drug status for the formulation. The decision to obtain a European Marketing Authorization was taken with the help of the OTT & PI, which signed an exclusive license agreement on the industrial development and commercialization of the drug with Laboratoires CTRS in 2007. Laboratoires CTRS then registered cholic acid as Orphacol<sup>®</sup> and obtained a Temporary Authorization for Use in France. On September 12, 2013, the orphan drug Orphacol<sup>®</sup> received European marketing authorization and gave new hope to the hundred or so eligible patients throughout Europe. Orphacol<sup>®</sup>'s efficacy and safety have been widely demonstrated. After a median treatment duration of 16 years, none of the patients have had to undergo liver transplantation and all have rapidly recovered a normal quality of life.

#### **About the AP-HP**

AP-HP, Assistance Publique - Hôpitaux de Paris, is the University Hospital Center (CHU) of Île-de-France (Paris and its suburbs) and the 1<sup>st</sup> University Hospital Center in Europe. Its 92,000 professionals are committed to providing all patients with high quality healthcare, 24h/24. 7 million people treated each year receive advanced treatment in all medical specialties. Created from the former Central Hospitals Pharmacy, the General Agency for Equipment and Health Products (AGEPS) implements the AP-HP's policy in terms of equipment and health products. It is a service provider to hospitals, and to the AP-HP's technical and pharmaceutical departments, with also national missions of general interest.

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#### **About OTT & PI**

The Office of Technology Transfer and Industrial Partnerships (OTT & PI) of the AP-HP protects and promotes innovations from all teams at the AP-HP and works in collaboration with AP-HP's Pharmaceutical Company to enhance innovations potential developed within it by providing expertise in development strategy: industrial property, definition of business models, search for industrial partners and investors for innovative projects development. [www.ottpi.aphp.fr](http://www.ottpi.aphp.fr)

#### **About CT-RS Laboratory**

Established in 2002, the CT-RS laboratory, a company incorporated under French law with exclusively private capital, develops, registers and markets products designed to treat rare and serious diseases for which there is only a very poor or nonexistent therapeutic approach. Quickly, the laboratory started to forge partnerships with academic structures with the aim of developing and advertising the richness of the French Research.

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