AOP Orphan Pharmaceuticals AG

Corporate Profile
THE COMPANY
AOP Orphan has acquired excellent expertise and developed a solid market presence thanks to its long-term experience. The fact that the company is privately owned ensures long-term commitment, high quality and continuity. AOP Orphan is also the sole provider of key therapies for a number of highly specialized indications.

AOP Orphan experts work closely with leading health care professionals on an international level. This enables them to respond quickly to new findings as well as to push both research and development projects forward. In the course of doing so, AOP Orphan can call upon a global network of qualified partners and, with the help of these strategic alliances, is able to compete with top pharmaceutical companies.

VISION AND STRATEGY
AOP Orphan’s vision developed from the experience of its founder, Dr. Rudolf Widmann, that patients with rare diseases are often ignored. Specialists in each of the small niche segments are hard to find and, for a long time, large pharmaceutical companies failed to dedicate any of their resources to rare diseases. AOP Orphan saw a viable opportunity to operate successfully in this segment – and therefore to help people afflicted by rare diseases.

The focus has been on product development ever since. At the same time, AOP Orphan has also been producing and distributing licensed products since its inception.

The company’s greatest asset lies in its close ties to research-oriented physicians, making it possible to conduct research with ongoing feedback and thereby provide patients with effective care.

AT A GLANCE
- Established in 1996
- Privately owned and owner-managed
- Headquarters in Vienna
- Offices in thirteen countries
- Over 200 employees
- Turnover in excess of EUR 95 million

EUROPEAN PIONEER
AOP Orphan researches, develops, produces and distributes innovative drugs and administration methods for rare diseases – and has become a European pioneer in the field of orphan diseases. Our focus is on the areas of hematooncology, cardiology and pulmonology, neurology and metabolic disorders.

“As a company, we are small enough to be really close to our patients, yet we are large enough to be able to provide them high-quality, personalized customer care.”

Dr. Rudolf Widmann
Chief Executive Officer
Chairman of the Board
THERAPEUTIC AREAS AND PRODUCT PORTFOLIO

THERAPEUTIC AREAS
AOP Orphan develops and commercializes complex, individualized solutions in the following therapeutic areas:

- Pulmonary arterial hypertension
- Arrhythmia/Tachycardia
- Essential thrombocythemia
- Chronic myelogenous leukemia
- Huntington’s disease
- Primary biliary cholangitis (PBC)
- Fragile-X-Syndrome
- Chemotherapy-induced nausea & vomiting (CINV)
- Cardiology & Pulmonology
- HematoOncology
- Neurology & Metabolic Disorders

PRODUCT PORTFOLIO
In the following areas: cardiology and pulmonology, hematooncology, neurology and metabolic disorders. AOP Orphan works tirelessly to increase its product portfolio for rare diseases.

<table>
<thead>
<tr>
<th>Cardiology &amp; Pulmonology</th>
<th>HematoOncology</th>
<th>Neurology &amp; Metabolic Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remodulin®</td>
<td>Thromboreductin®</td>
<td>Nabilone AOP 2020</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension</td>
<td>Essential thrombocythemia</td>
<td>Pain medication</td>
</tr>
<tr>
<td>Rapibloc®</td>
<td>Hemitransplantation</td>
<td>Prokinetic schizophrenia</td>
</tr>
<tr>
<td>Allows rapid control of heart rate with a straightforward dosing scheme in a variety of perioperative and intensive care situations</td>
<td></td>
<td>Fradaise®: Moderate agitation (Schizophrenia/Bipolar disorder)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Feraccru®: Iron deficiency anemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ocaliva®: Primary biliary cholangitis (PBC)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Canemes®: Chemotherapy-induced nausea &amp; vomiting (CINV)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nabilone AOP 2020</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anagrelide prolonged release**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ocaliva®: Primary biliary cholangitis (PBC)</td>
</tr>
</tbody>
</table>

** Only Named Patient Basis
Note: The medicinal products listed may not be authorized for marketing in every country listed in this brochure

RESEARCH AND DEVELOPMENT
AOP Orphan invests a large share of its turnover in research and development, operating at an international level in doing so. Research is conducted across Europe, with a particular focus on Central Europe, and covers the entire range of different development stages.

The company performs both early clinical trials and multinational pivotal trials with patients in the whole of Europe. Furthermore, clinical studies are performed with already approved products in order to optimize administration or to make the drug available to other groups of patients.

PIPELINE
In addition to its current portfolio, AOP Orphan also has a very promising product development pipeline, which is set to deliver a number of market-ready products in the next few years. These range from a particularly fast-acting beta blocker for tachycardic patients to ropeginterferon alfa-2b for patients with Polycythemia vera, a bone marrow disorder characterized by overproduction of red blood cells.

<table>
<thead>
<tr>
<th>Cardiology &amp; Pulmonology</th>
<th>HematoOncology</th>
<th>Neurology &amp; Metabolic Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trade name/active ingredient</td>
<td>Remodulin®</td>
<td>Nabilone</td>
</tr>
<tr>
<td>Pharmacotherapeutic group/Mode of action</td>
<td>Pulmonary arterial hypertension</td>
<td>Pain medication</td>
</tr>
<tr>
<td>Indication</td>
<td>Essential thrombocythemia</td>
<td>Fradaise®: Moderate agitation (Schizophrenia/Bipolar disorder)</td>
</tr>
<tr>
<td>Phase</td>
<td>Approved EU Filing USA 2019</td>
<td>Investigator initiated studies II</td>
</tr>
</tbody>
</table>

Although AOP Orphan does not have its own laboratories or production facilities, it can resort to a global network of professional partners and service providers. Moreover, the company’s own research team covers every key aspect relating to product development, ranging from pre-clinical research and toxicology to pharmaceutical development, clinical development, regulatory affairs, quality management and pharmacovigilance. Experts in the individual areas of specialization work as project managers in close cooperation with each other and with external service providers and partners to implement the ambitious research projects.
RECENT PUBLICATIONS

ROPEGINTERFERON ALFA-2B

Ropeginterferon Alfa-2b Induces High Rates of Clinical, Hematological and Molecular Responses in Polycythemia Vera: Two-Year Results from the First Prospective Randomized Controlled Trial
Heinz Gisslinger • et al. American Society Hematology ASH Annual Meeting 2017, oral presentation

Molecular response to hydroxyurea and ropeginterferon alfa-2b in the PROUD-PV randomized phase 3 trial
Jean-Jacques Kiladjian • et al. European Hematology Association EHA Annual Meeting 2017, oral presentation

Final results from PROUD-PV a randomized controlled phase 3 trial comparing Ropeginterferon alfa-2b to hydroxy urea in Polycythe- 
ma vera patients
Heinz Gisslinger • et al. American Society Hematology ASH Annual Meeting 2016, oral presentation

Ropeginterferon alfa-2b, a novel IFNα-2b, induces high response rates with low toxicity in patients with polycythemia vera

Molecular responses and chromosomal aberrations in patients with polycythemia vera treated with peg-proline-interferon 
alpha-2b

ANAGRELIDE RETARD

Pharmacokinetics of a novel, Anagrelide extended-release formulation delivered with different food intake in healthy subjects analyzed by a randomized, 3-way crossover trial
Petro E. Petrides • et al. Clinical Pharmacology in Drug Development, 7 (2):129 -131, 2018

Final results from the Phase 3 trial ARETA comparing a novel, extended-release anagrelide formulation to placebo in Essential 
Thrombocythemia patients with defined risk status
Heinz Gisslinger • et al. American Society Hematology ASH Annual Meeting 2016, oral presentation

Phase 3 trial TEAM-ET in 106 high-risk Essential Thrombocythemia patients, demonstrating non-inferiority of Anagrelide Retard, a novel, extended-release anagrelide formulation, to the licensed comparator
Heinz Gisslinger • et al. European School of Hematology EHA 21st Congress, Jun 9-12, 2016

LANDIOLOL

Pharmacokinetics and -dynamics of low, intermediate and high dose landiolol and esmolol during long term infusion in healthy Caucasians
Günther Krumpl • et al. J Cardiovasc Pharmacol. 71(3): 137-146, 2018

Pharmacodynamic and -kinetic Behavior of Low-, Intermediate-, and High-Dose Landiolol During Long-Term Infusion in Whites

Bolus application of landiolol and esmolol: comparison of the pharmacokinetic and pharmacodynamic profiles in a healthy Cauca-
sian group.

Pharmacokinetics and pharmacodynamics of two different landiolol formulations in a healthy Caucasian group.

MARKETS AND LOCATIONS

The Vienna-based company has been expanding towards Central and Eastern Europe with increasing success. Today AOP Orphan operates in all five continents. The rare diseases specialist has branch offices situated in its core markets within Europe and the Middle East. The international markets are handled and operated by long-term, close partners of the company.
PARTNERING
AOP Orphan researches, develops, produces and distributes innovative drugs and therapeutic solutions. At the same time, however, partnerships are very important – both in the field of research and in the market.

RESEARCH PARTNER
AOP Orphan is heavily involved in research and development activities and can therefore be a highly competent partner for other companies. A well-staffed research department, broad detailed knowledge and close ties to study centres are of particular value here. As a fully integrated pharmaceutical company, AOP Orphan conducts phase I to phase IV clinical trials also for and together with partners. A good example are the two studies PEGINVERA and PROUD-PV, in the course of which ropeginterferon alfa-2b is being tested as a treatment for polycythemia vera.

MARKET PARTNER
AOP Orphan knows about the intricacies of doing business in the markets of Europe and the Middle East. Mentalities, cultures, healthcare systems and, above all, legal frameworks are so different that a superficial knowledge of the market is not enough. This is why AOP Orphan is present in each of its core markets with its own employees in order to meet these challenges properly. These include cultural understanding, marketing know-how, cost and approval know-how, compliance and specific knowledge in the field of health technology assessment.

IN-LICENSING AND OUT-LICENSING
For AOP Orphan, partnerships can take two forms – as a partner for pharmaceutical companies looking to place their product in AOP Orphan’s core markets (in-licensing) and as a licensor for in-house developments that will be distributed by partners in other countries (out-licensing). In both cases, a trusting collaboration is based on having equal footing as well as demonstrating seriousness, expertise and passion for the matter at hand. Partnerships concentrate essentially on the key treatment areas of cardiology & pulmonology, hematology & oncology, and neurology & psychiatry. In addition to this, AOP Orphan is also open to other treatment areas in the field of rare diseases as well as for special products.

The complexity of the treatment areas requires long-term cooperation with all stakeholders in the healthcare system. For this reason, partnerships are usually designed to continue for an extended period of time within the product life cycle.

For AOP Orphan, in-licensing means obtaining exclusive marketing rights for a product in a specific region – preferably in the core markets of the United Kingdom, Austria, France, Germany, Switzerland, the Baltic states, Poland, Czech Republic, Slovakia, Hungary, Slovenia, Croatia, Bosnia-Herzegovina, Romania, Bulgaria, Turkey, Scandinavia and the Middle East. In addition to these markets, AOP Orphan is also active in Belarus, Ukraine, Russia and Kazakhstan.

Within the framework of out-licensing, AOP Orphan issues marketing rights for products developed in-house. This relates particularly to regions where AOP Orphan does not pursue any commercial activities with its own employees. Such regions mainly include North and South America, Africa, South-East Asia, Australia and Russia.

“Finding solutions for apparently impossible tasks, always focusing on the patients with a deep appreciation of their disease experience makes AOP Orphan a unique partner.”
Agnes Kohl, MPharmSc
Head of Business Development