



**HUVEPHARMA<sup>®</sup>**  
ITALIA S.R.L.



**HUVEPHARMA<sup>®</sup>**  
We add performance to your business

v. Sept. 2018

# 1 | Global Organization



- **Huvepharma ITALIA S.R.L.** is a newly established company, 100% owned by Huvepharma EOOD, a private Bulgarian company owned by the Domuschiev family.
- **Huvepharma EOOD** is a fast growing, pharmaceutical company globally organized to develop, manufacture and commercialize products for human and animal health.

**HUVEPHARMA** stands for:

**HU**man &

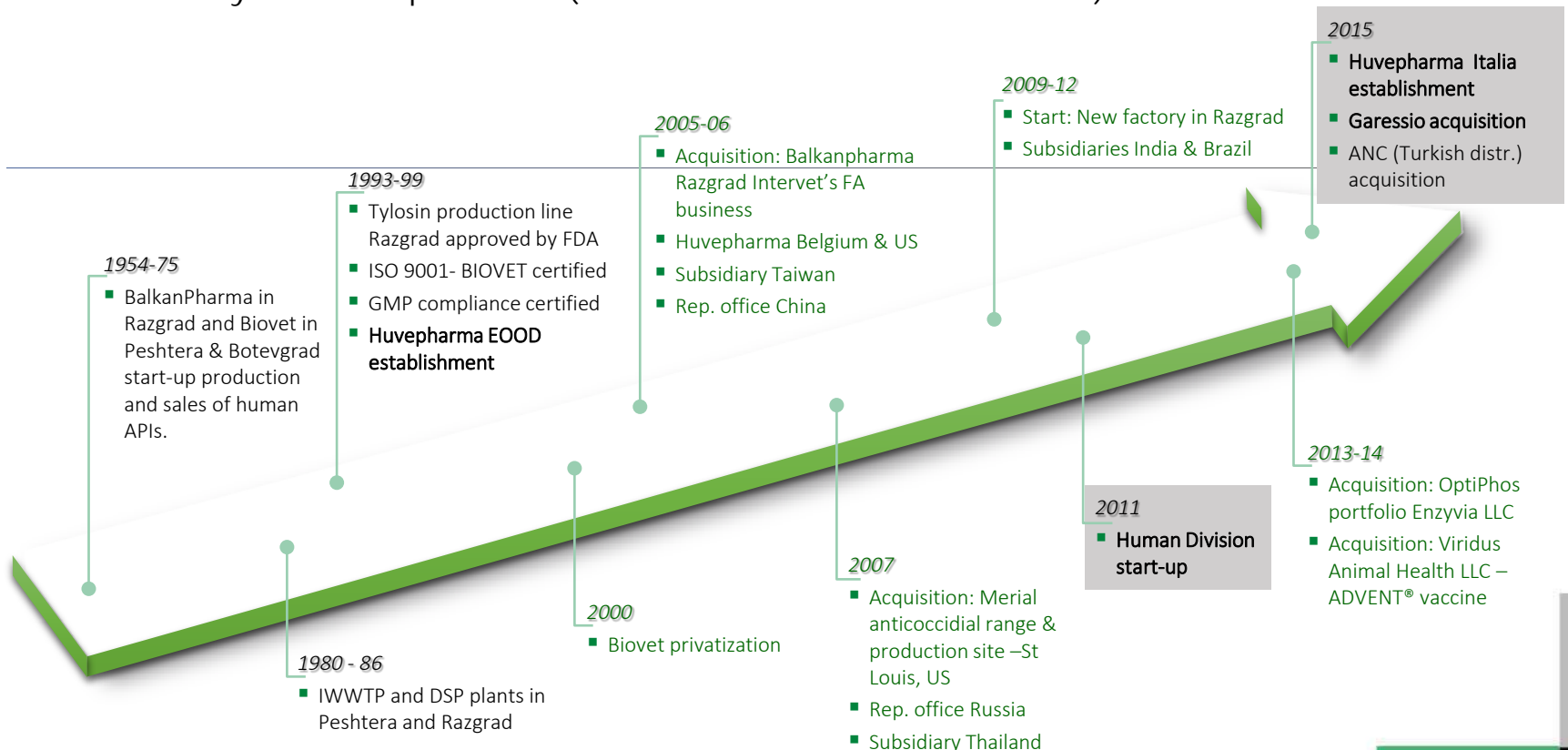
**VE**terinary

**PHARMA**ceuticals

- **Huvepharma ITALIA S.R.L.** was established in 2015 with the acquisition of the Sanofi facility located in Garessio (CN).
  
- **Huvepharma ITALIA S.R.L.'s** focus is the development, production and commercialization of advanced intermediates and API manufactured by chemical synthesis.
  
- **Huvepharma ITALIA S.R.L.'s** plan is to:
  - invest in high-potency development and production assets,
  - complete the strategic offer for start-up companies looking for qualified and FDA approved companies,
  - be reliable and qualified partner from Phase 1 through commercial phase.



**Huvepharma EOOD** is a young European company (founded in 1999), nevertheless possessing consolidated and recognized fermentation knowhow and capabilities owing to the acquisition of companies with over 60 years of experience (f.ex.: BalkanPharma and Biovet).





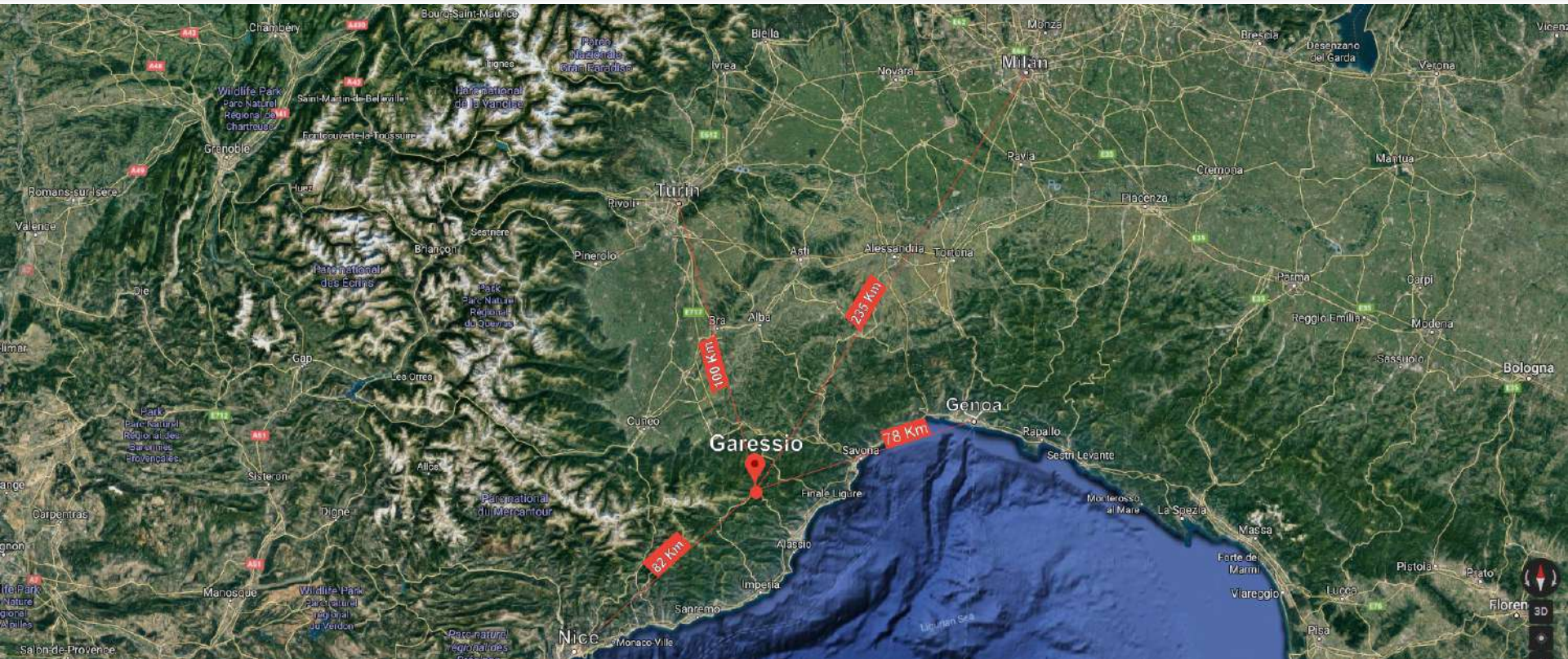
## 2 | Garessio Facilities



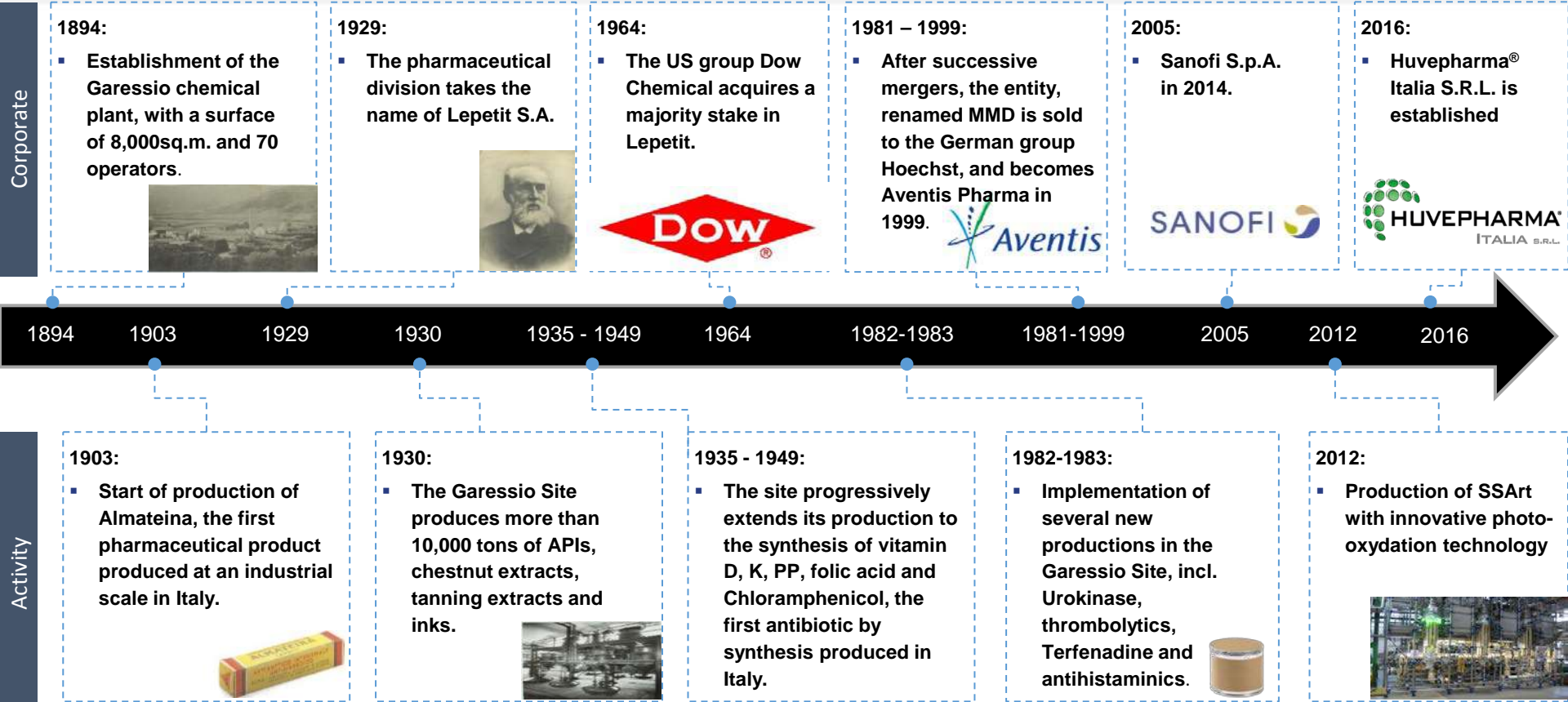


The Garessio facility is specialized in the development, industrialization and production of Active Pharmaceutical Ingredients and API-intermediates via synthetic chemistry





The facility is located in NW Italy,  
well connected to multiple international Airports



Long-established player in the pharma-chemical market with a strongly recognized experience in introducing and developing new technologies

# 3 | Capabilities & Strengths

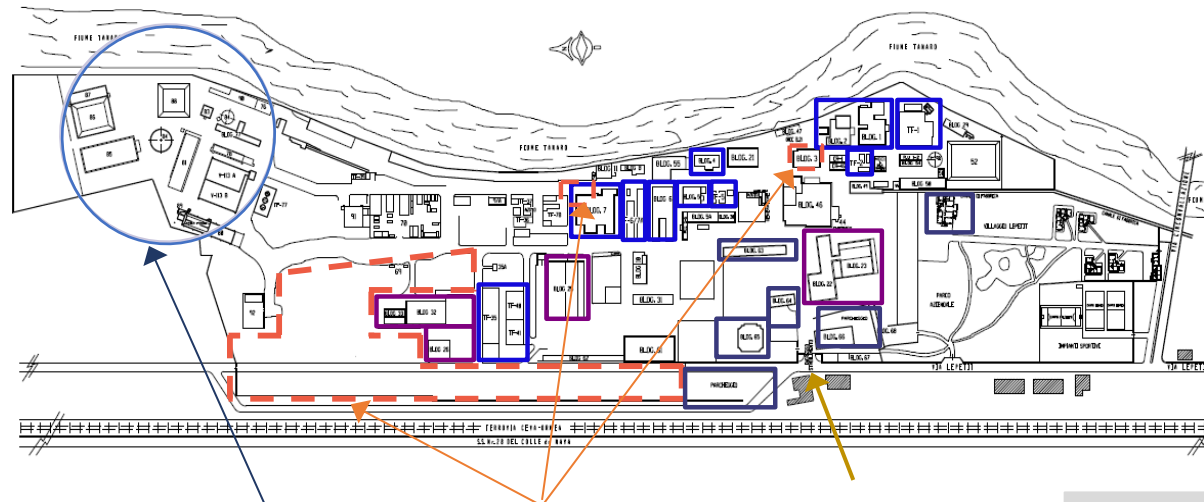


# Capabilities & Strengths

An autonomous asset with room for expansion

## Production Facilities

5 production bldgs.  
8 production lines  
3 Solvents recovery units  
100 reactors (total vol. 700 cu.m)  
97 tanks (3,000 m<sup>3</sup>) in several tank farms



Waste treatment

Expansion areas  
(27,500 m<sup>2</sup>)

Main entrance

Property:  
264,000 m<sup>2</sup>

## Expansion Areas

Available plot of land of 27,500sq.m.  
Building 3 currently unused  
Expansion area in Building 7 (with a part currently unused)

## R&D Facilities

Equipped labs.  
1 pilot building  
1 very flexible pilot line

## Warehouses

8 warehouses

## Other Facilities

Administration: site direction, engineering, quality, HR, controlling  
Canteen  
Parking  
Guest house  
WWTP  
Thermal Oxidizer

# Capabilities & Strengths

Excellence in process and in technologies

- ❑ **Complex chemical reactions in large scale:**
  - ❑ Catalytic hydrogenations (homogeneous, etherogeneous)
    - ❑ various catalysts (Ru, Rh, Pd)
    - ❑ up to 50 bar
    - ❑ up to 10 m<sup>3</sup>
  - ❑ Catalytic carbonylation with CO gas
  - ❑ Grignard reactions, up to 8 cu m
  - ❑ Friedel Crafts
  - ❑ Gas liquid reactions (by HCl gas)
  - ❑ Peroxide handling (RM, intermediates and finished products)
  - ❑ **Photo-oxidation**
  - ❑ **Bromination**
- ❑ **Crystallization controlled by Fiber Optics**
- ❑ **Separation of optical isomers**
- ❑ **Production lines 50% computerized**
- ❑ **Cogeneration, thermal-electrical (back pressure turbine)**

**In addition to the Pilot Plant building with relatively small scale equipment: 19 SS and glass lined reactors (total 59 m<sup>3</sup>), hastelloy centrifuge and dryer, clean packaging room:**

- ❑ Process Development Laboratories: two laboratories dedicated to development activities with HPLC, GC, etc.
- ❑ Process development / optimization
- ❑ Analytical method development
- ❑ Stability program for API and Intermediates
- ❑ Reference standards preparation expertise
- ❑ Process validation

# Capabilities & Strengths

Consolidated and qualified Quality organization

## Quality Control

- Sampling
- Testing and Release of RMs
- Release tests for INT and API
- In-process control
- Reference Standards management
- Retained samples
- Stability programs

## Quality Assurance

- Release INT and API
- Batch record review
- Deviation management
- Validation and Qualification
- Annual Product Review
- SOPs management
- Change control management
- Suppliers management
- GMP training

## Regulatory

- Regulatory documentation (DMFs, CEPs, Abridged Dossiers)
- SMF management
- Change Control assessment

# Capabilities & Strengths

...resulting in excellent regulatory reputation

<b>GMP inspection date</b>	<b>Regulatory Agency</b>	<b>Country</b>
11-15 May 2019	FDA	USA
18-21 October 2011	AIFA	Italy
24-26 October 2012	AIFA	Italy
12-16 November 2012	FDA	USA
21-25 September 2015	AIFA	Italy
15-19 February 2016	FDA	USA







# Capabilities & Strengths

.... And strong attention to HSE - Environmental certification ISO 14001:2015



CERTIFICATO N. 2429  
CERTIFICATE No

SI CERTIFICA CHE L'ORGANIZZAZIONE  
WE HEREBY CERTIFY THAT THE ORGANIZATION

**HUVEPHARMA ITALIA S.r.l.**

IT - 12075 GARESSIO (CN) - VIA R.LEPETIT 142

NEI SEGUENTI SITI / IN THE FOLLOWING SITES  
IT - 12075 GARESSIO (CN) - VIA R. LEPETIT 142

HA ATTUATO E MANTIENE UN SISTEMA DI GESTIONE AMBIENTALE CHE SI CONFORMA ALLA NORMA  
HAS IMPLEMENTED AND MAINTAINS AN ENVIRONMENTAL MANAGEMENT SYSTEM WHICH COMPLIES WITH THE FOLLOWING STANDARD:

**UNI EN ISO 14001:2015**

PER LE SEGUENTI ATTIVITÀ / FOR THE FOLLOWING ACTIVITIES SETTORE **IAF 13, 12**

Produzione di intermedi e principi attivi farmaceutici via sintesi chimica. Stoccaggio di materie prime sfuse ed a collette. Stoccaggio e spedizione di prodotti finiti sfusi ed a collette.  
*Production of intermediates and pharmaceutical active ingredients by chemical synthesis. Stocking of raw materials, loose and packaged. Stocking and shipment of finished products, loose and packaged.*

Certificazione rilasciata in conformità al Regolamento Tecnico ACCREDIA RT 09

IL PRESENTE CERTIFICATO È SOGGETTO AL REGIMENTO DEL RINNOVAMENTO PER LA CERTIFICAZIONE DEI SISTEMI DI GESTIONE  
THIS LIST AND THE VALIDITY OF THE CERTIFICATE SHALL SATISFY THE REQUIREMENTS OF THE RULES FOR THE CERTIFICATION OF MANAGEMENT SYSTEMS

PRIMA EMISSIONE: 20/12/1999  
FIRST ISSUE: 20/12/1999  
DATA DEL RINNOV: 06/02/2018  
RENEWAL DATE: 06/02/2018  
DATA SCADENZA: 10/02/2021  
EXPIRY DATE: 10/02/2021  
EMISSIONE CORRENTE: 06/02/2018  
ISSUE DATE: 06/02/2018

*Emerto Offici*  
CERTIQUALITY S.r.l. PRESIDENTE  
Via S. Stefano 4 - 20123 Milano (MI) - ITALY



After, the association of the world's top class certification bodies, is the largest provider of management system certification in the world (IQNet is composed of more than 50 bodies and covers more than 120 countries of all over the globe)

For information concerning the validity of the certificate please visit the site: www.iqnet-certification.com

The validity of the certificate depends on correct audit and on a continuous review every three years of the Management System.



THE INTERNATIONAL CERTIFICATION NETWORK

**CERTIFICATE**

CISQ/CERTIQUALITY S.r.l.  
has issued an IQNet recognised certificate that the organization:

**HUVEPHARMA ITALIA S.r.l.**

IT - 12075 GARESSIO (CN) - VIA R.LEPETIT 142  
for the following scope

Production of intermediates and pharmaceutical active ingredients by chemical synthesis. Stocking of raw materials, loose and packaged. Stocking and shipment of finished products, loose and packaged.

has implemented and maintains a  
**Environmental Management System**  
which fulfills the requirements of the following standard  
**ISO 14001:2015**

Issued on: 2018-02-06  
First issued on: 1999-12-20  
Expires on: 2021-02-10

This attestation is directly linked to the IQNet Partner's original certificate and shall not be used as a stand-alone document

Registration number: **IT-10005**



*Alex Stoichitov*  
Alex Stoichitov  
President of IQNET



*Ing. Claudio Provetto*  
Ing. Claudio Provetto  
President of CISQ

**IQNet Partners\*:**

AENOR Spain AFNOR Certification France APCER Portugal CCC Cyprus CISQ Italy  
CQC China CQM China CQS Czech Republic Cn Cert Croatia DQS Holding GmbH Germany FCAV Brazil  
FONDONORMA Romania ICOTEC Colombia Inspecta Scandinavia Oy Finland INTECO Costa Rica  
IRAM Argentina IQA Japan KFQ Korea MIRTEC Greece MSZT Hungary Nemko AS Norway NSAI Ireland  
NYCE-SIGE Mexico PCBC Poland Quality Austria Austria B.R. Russia SII Israel SIQ Slovenia  
SIRIM QAS International Malaysia SQS Switzerland SRAC Romania TEST St Petersburg Russia TSE Turkey YUQS Serbia  
IQNet is represented in the USA by: AFNOR Certification, CISQ, DQS Holding GmbH and NSAI Inc.

\* The list of IQNet partners is valid at the time of issue of this certificate. Updated information is available under www.iqnet-certification.com

# Capabilities & Strengths

.... And strong attention to HSE - Safety certification ISO 18001:2007



**THE INTERNATIONAL CERTIFICATION NETWORK**

## CERTIFICATE

IQNet and its partner  
**CISQ/CERTIQUALITY S.r.l.**

**HUVEPHARMA ITALIA S.r.l.**

IT - 20079 SAN DONATO MILANESE (MI) - VIALE DELLA LIBERTA' 80  
has implemented and maintains a  
**Safety Management System**  
which fulfills the requirements of the following standard  
**OH SAS 18001:2007**  
for the following activities Code **IAF 12**  
Production of intermediates and active pharmaceutical ingredients.

in the following operative units  
IT - 12075 GARESSIO (CN) - ROBERTO LEPETIT 142

Issued on: **2016-09-26**  
Certified since: **2007-12-13**  
Expire on: **2019-08-02**  
Registration number: **IT-62306**



CERTIFICATO n. **12044**  
CERTIFICATE No

SI CERTIFICA CHE L'ORGANIZZAZIONE  
WE HEREBY CERTIFY THAT THE ORGANIZATION

**HUVEPHARMA ITALIA S.r.l.**

IT - 20079 SAN DONATO MILANESE (MI) - VIALE DELLA LIBERTA' 80

NEI SEGUENTI SITI / IN THE FOLLOWING SITES  
IT - 12075 GARESSIO (CN) - ROBERTO LEPETIT 142

HA ATTUATO E MANTIENE UN SISTEMA DI GESTIONE SICUREZZA CHE E' CONFORME ALLA NORMA  
HAS IMPLEMENTED AND MAINTAINS A SAFETY MANAGEMENT SYSTEM WHICH COMPLES WITH THE FOLLOWING STANDARD

**OHSAS 18001:2007**

PER LE SEGUENTI ATTIVITA' / FOR THE FOLLOWING ACTIVITIES SETTORE / IAF 12

Produzione intermedi e principi attivi farmaceutici.  
*Production of intermediates and active pharmaceutical ingredients.*

CISQ is a member of



www.iqnet-certification.com

IQNet, the association of the world's best chief certification bodies, is the largest provider of management System Certification in the world. IQNet is composed of more than 30 bodies and counts over 110 laboratories all over the globe.



*Michael Drechsel*  
President of IQNET



*Ing. Claudio Provetti*  
President of CISQ

**IQNet Partners\*:**  
AENOR Spain AFNOR Certification France AIB-Vincotte International Belgium APCER Portugal CCC Cyprus  
CISQ Italy CQC China CQM China CQS Czech Republic Cro Cert Croatia DQS Holding GmbH Germany  
FCAV Brazil FONDONORMA Venezuela ICONTEC Colombia IMNC Mexico Inspecta Certification Finland INTECO Costa Rica  
IRAM Argentina JQA Japan KFQ Korea MIRTEC Greece MSZT Hungary Nemko AS Norway NSAI Ireland PCBC Poland  
Quality Austria RR Russia SIGE Mexico SII Israel SIQ Slovenia SIRIM QAS International Malaysia  
SQS Switzerland SRAC Romania TEST St Petersburg Russia TSE Turkey YUQS Serbia  
IQNet is represented in the USA by: AFNOR Certification, CISQ, DQS Holding GmbH and NSAI Inc.

\* The list of IQNet partners is valid at the time of issue of this certificate. Updated information is available under [www.iqnet-certification.com](http://www.iqnet-certification.com)

Certificazione rilasciata in conformità al Regolamento Tecnico SINCERT 81/12  
THE USE AND THE VALIDITY OF THE CERTIFICATE SHALL SATISFY THE REQUIREMENTS OF THE RULES FOR THE VERIFICATION OF MANAGEMENT SYSTEMS

PRIMA EMISSIONE / FIRST ISSUE	13/12/2007
EMISSIONE CORRENTE / CURRENT ISSUE	26/09/2016
DATA SCADENZA / EXPIRY DATE	02/08/2019

*Esposito*  
CERTIQUALITY S.r.l. IL PRESIDENTE  
Via G. Sestini 4 - 20133 MILANO (MI) - ITALY



CONFERENZA ITALIANA ACCREDITAMENTO  
Riconoscimento EA, IAF e IAC  
Registry of EA, IAF and IAC Bodies  
Accreditation Agreements



www.cisq.com

CISQ è la Federazione Italiana di Organismi di Certificazione dei sistemi di gestione aziendale. CISQ is the Italian Federation of management System Certification Bodies.

# Capabilities & Strengths

.... And strong attention to HSE - Seveso certification UNI 10617



CERTIFICATO n. **23818**  
CERTIFICATE No

SI CERTIFICA CHE L'ORGANIZZAZIONE  
WE HEREBY CERTIFY THAT THE ORGANIZATION

**HUVEPHARMA ITALIA S.r.l.**

IT - 20079 SAN DONATO MILANESE (MI) - VIALE DELLA LIBERTA' 80

NEI SEGUENTI SITI / IN THE FOLLOWING SITES

IT - 12075 GARESSIO (CN) - ROBERTO LEPETTIT 142

HA ATTUATO E MANTIENE UN SISTEMA DI GESTIONE SICUREZZA CHE SI CONFORMA ALLA NORMA  
HAS IMPLEMENTED AND MAINTAINS A SAFETY MANAGEMENT SYSTEM WHICH CONFORMS WITH THE FOLLOWING STANDARD

**UNI 10617**

PER LE SEGUENTI ATTIVITA' / FOR THE FOLLOWING ACTIVITIES: SETTORE  
CODE **IAF 13**

Produzione intermedi e principi attivi farmaceutici.  
*Production of intermediates and pharmaceutical active ingredients.*

IL PRESENTE CERTIFICATO E' SOGGETTO AL RISPETTO DEL REGOLAMENTO PER LA CERTIFICAZIONE DEI SISTEMI DI GESTIONE  
THE USE AND PREVALENCY OF THE CERTIFICATE SHALL SATISFY THE REQUIREMENTS OF THE RULES FOR THE CERTIFICATION OF MANAGEMENT SYSTEMS

PRIMA EMISSIONE FIRST ISSUE	03/08/2016
EMISIONE CORRENTE CURRENT ISSUE	26/09/2016
DATA SCADENZA EXPIRY DATE	01/09/2018



CERTIQUALITY S.r.l. - IL PRESIDENTE  
Via G. Galvani 4 - 20123 MILANO (MI) - ITALY

CISQ is a member of



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For information concerning the validity of the certificate, you can visit the site [www.ionet-certification.com](http://www.ionet-certification.com)

The validity this certificate depends on general audit and on a compliance review every three years of the Management System.



FEDERAZIONE  
**CISQ**  
[www.cisq.com](http://www.cisq.com)

CISQ è la Federazione Italiana di Organismi di Certificazione dei sistemi di gestione aziendali.  
CISQ is the Italian Federation of management system Certification Bodies.

# Capabilities & Strengths

... And strong attention to HSE - ECOVADIS 2018 evaluation



**ecoVadis**  
SUSTAINABLE SUPPLY MANAGEMENT  
Corporate Social Responsibility (CSR)

**HUVEPHARMA ITALIA SRL**  
has been granted a  
**Silver Recognition Level**  
Based on their EcoVadis CSR rating  
April 2018

2018  
CSR Rating  
SILVER  
ecoVadis

*[Signature]*  
ECOVDIS SAS  
11000 Courmayeur - 11010 Courmayeur - 11010 Courmayeur - France  
0033 477 811 914 - 0033 477 811 914

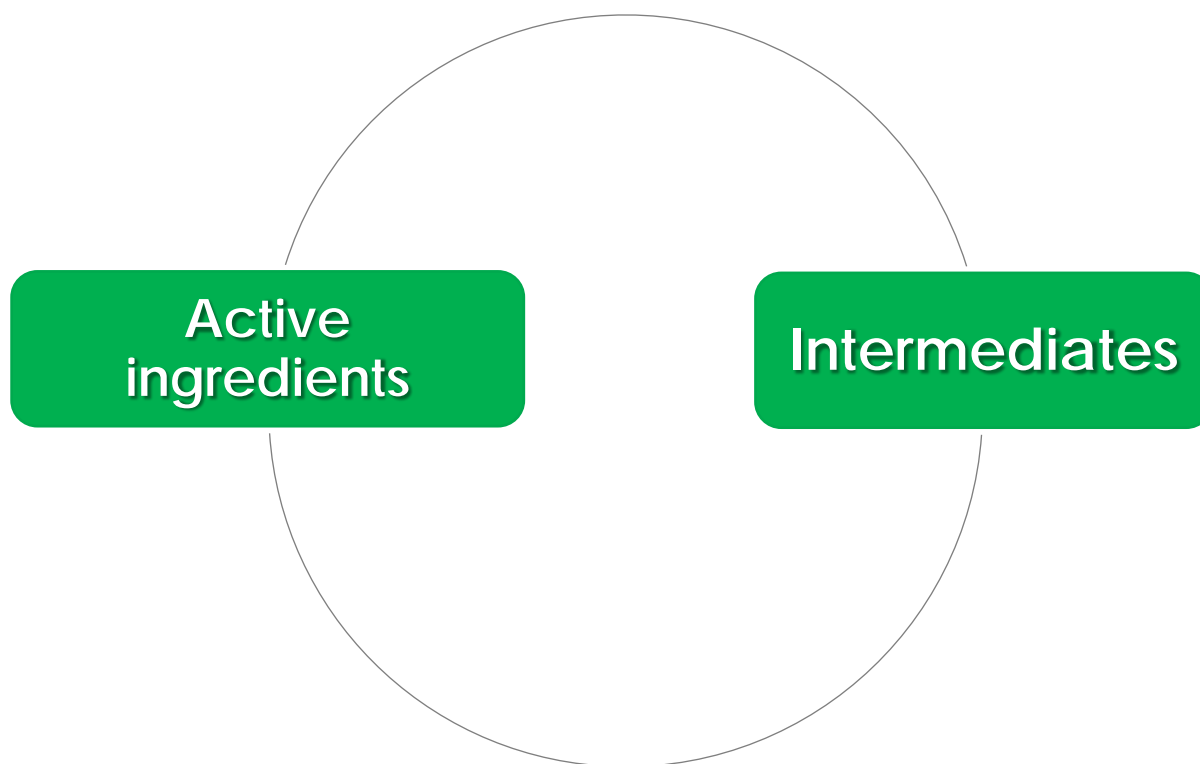
Valid until : April 2019

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# 5 / Product Portfolio





<b>Artesunate</b>	•anti-malaria   CAS n. 88495-63-0	Filed to FDA, WHO approved
<b>Oxybutynin HCl</b>	•anticholinergic   CAS n. 1508-65-2	PMDA accredited
<b>Antiepileptic</b>	•toll manufacturing	FDA approved
<b>Artemether</b>	•anti-malaria CAS n. 71963-77-4	WHO approved
<b>ASK2 - Potassium N-acetylaminosuccinate</b>	•nootropic CAS n. 3397-52-2	
<b>Tiapride HCl</b>	•neurological and psychiatric disorders   CAS n. 51012-33-0	CEP available
<b>Sulpiride</b>	•antipsychotic CAS n. 15676-16-1	CEP available
<b>Halofuginone</b>	•captive use	
<b>Ractopamine</b>	•captive use	
<b>Deflazacort</b>	•anti inflammatory CAS n. 14484-47-0   dev. phase	



### Chloro 2 phenothiazine

- CAS n. 92-39-7 (Chlorpromazine/Cyamemazine)

### Semisynthetic Artemisinin

- CAS n. 63968-64-9 (antimalaria APIs) WHO approved

### Cis triol acetone

- CAS n. 52187-19-6 (Nadolol)

### Cortiseven

- CAS n. 21269-13-6 (Deflazacort)

### Ramipril Precursor 1

- CAS n. 82717-96-2 (Ramipril, Enalapril, etc.)

### Thiophene Ester Base

- CAS n. 85006-31-1 (Articaine)

### Food Fragrance

- (toll manufacturing)

### Anidulafungin

- CAS n. 166663-25-8 (anti-fungal)

### Azacyclonol free base

- CAS n. 115-46-8 (Fexofenadine)





# 6 | Conclusion



# Our Competitive Advantage

Huvepharma Italia is a recognized partner offering:

## Excellent regulatory reputation

- Sites that operate under high quality standards (FDA & AIFA approvals; OHSAS 18001 & ISO 14001 certifications)

## Flexible & fast response

- Consolidated experience in collecting all data & process information from the start for easy regulatory submission.

## Chemistry & fermentation cost competitive expertise

- Strong experience in implementing new productions & new technologies
- In addition to Garessio facility expertise in chemical synthesis, Huvepharma Italia takes advantage of the fermentation expertise & cost effectiveness of the Bulgarian manufacturing plants.

## Confidentiality

- A key policy of the Huvepharma Group



**THANK YOU  
FOR YOUR ATTENTION**

