

## CONTACT

### ZELLER INTERNATIONAL

We are constantly looking to expand our international activities through long-term cooperation with global and local licence partners. If this is of interest to your company or should you require further information on Zeller or Zeller products, please feel free to contact our international business unit at:

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Swiss expertise in phyto-pharmaceuticals  
since 1864





## MAX ZELLER SÖHNE AG

Max Zeller Söhne AG specialises in the development, production and marketing of phyto-pharmaceuticals with clinically proven efficacy, safety and tolerability.

We are a Swiss family-owned phyto-pharmaceutical company in the fifth generation. Over the past 150 years, our company has grown from a small pharmacy in Romanshorn to a manufacturer of “state-of-the-art” medicines. Today, we are the leader in the Swiss market for phyto-pharmaceuticals and one of the few companies that controls the entire value chain from seed to patient.

At our sites in Romanshorn and Uttwil (Vitaplant), 135 employees in diverse disciplines such as biology, agriculture, process engineering, pharmacy and medicine are committed to develop the highest quality, evidence-based medicine.

Patients benefit from Zeller phyto-pharmaceuticals both in Switzerland and worldwide.



*“We develop innovative phyto-pharmaceuticals for selected indication areas to improve patients’ health and quality of life.”*

*Dr. Georg Boonen, CEO*

## MISSION, PHILOSOPHY, VALUES

We manufacture phyto-pharmaceuticals that meet the highest standards of modern medicine.

We use state-of-the-art scientific methods to develop phyto-pharmaceuticals with the highest efficacy, safety and tolerability.

We continuously improve and broaden research and development competences in-house and in collaboration with academic institutions worldwide.

We are dedicated to continuously refine our seed to patient process to guarantee highest quality and batch-to-batch consistency.



### BEGINNINGS

Paul Friedrich Gaupp and Max Zeller opened the first Zeller pharmacy in Romanshorn in 1864 followed by another two pharmacies. For the early manufacture of herbal preparations, Max Zeller used plants grown by local farmers.

### ZELLER WONDERBALM

The first Zeller product was a so-called "Wonderbalm" (Zeller Balm) which became extremely popular as a herbal remedy for the treatment of gastro-intestinal complaints. Wonderbalm consisted of carefully selected medicinal plants (aromatic resins, roots, barks and blossoms) to which antispasmodic, anti-inflammatory, analgesic and digestive effects were attributed. Interest from abroad led to the rapid success of the Wonderbalm and soon it was sold in 14 countries. In the 1950s, sales of the Wonderbalm reached several million units worldwide.

*1864: First Zeller Pharmacy in Romanshorn*



### GROWTH

At the beginning of the 20<sup>th</sup> century, Max Zeller's sons followed in their father's footsteps and the company became the partnership Max Zeller Söhne. From then on, medicinal plants were no longer obtained from Switzerland only but also from Africa and India. The acquisition of a factory building in 1920 meant the beginning of the industrial manufacture of phyto-pharmaceuticals. The first assembly line went into operation after the Second World War in 1949. The company tripled the output over the following 10 years and grew to 70 employees.

### PHARMA BUSINESS

The factory was supplemented in 1977 by a laboratory for both research and development (R&D) as well as quality control. Despite Zeller's growth, it became clear that Zeller was still too small to be able to finance the increasingly important R&D and the corresponding technology. As a result, a coopera-

*Headquarters of Max Zeller Söhne AG in Romanshorn*



## ZELLER HISTORY

tion with Ciba-Geigy (now Novartis) was initiated in 1985. Academic collaborations with universities such as ETH Zurich and the Universities of Basel and Bern were established at this time and these continue until today. Zeller allocates about 15% of the annual turnover to R&D.

### ZELLER TODAY

To complement the existing Zeller OTC business in Switzerland, Zeller Medical AG, a business unit dedicated to the close collaboration with physicians, was founded in 1996. Today, Zeller OTC and Zeller Medical represent the cornerstone for evidence-based phyto-therapy in Switzerland. In addition, our products are registered and distributed in a number of markets worldwide.

# EVIDENCE-BASED PHYTO-THERAPY

## HERBAL MEDICINE YESTERDAY AND TODAY

Remedies made from plants have been known to humans for thousands of years and are common in every culture. Before chemical synthetic drugs became available at the beginning of the 20th century, the use of medicinal plants as pharmaceuticals (phyto-therapy) was the only way to alleviate complaints and cure diseases. For these traditional remedies, empirical knowledge was the only proof of efficacy.

Today, healthcare professionals differentiate between traditional remedies and rational phyto-pharmaceuticals based on clinical evidence, which is widely accepted as

part of modern pharmacotherapy. In the manufacturing of phyto-pharmaceuticals, the process defines the product. Therefore, each herbal extract is unique even if it derived from the same plant. A lot of expertise is required to guarantee batch-to-batch consistency at each step of the production.

As a modern phyto-pharmaceutical company, we are committed to deliver the highest quality evidence-based, rational phyto-therapy. Numerous (pre-) clinical and post-marketing studies prove the efficacy, safety and tolerability of Zeller products. Our high standards make our products the preferred choice in the first-line treatment among healthcare professionals and patients.



## AGRO COMPETENCE

Herbal raw materials for pharmaceutical use contain biologically active compounds and must meet the highest quality standards. To guarantee this, Vitaplant AG, a fully owned subsidiary of Zeller AG, specialises in the developing and ensuring sustainable production of high-quality medicinal plants.

Besides the procurement of Zeller with highest quality raw material, Vitaplant provides its services to third party companies in the pharmaceutical, nutrition, animal-feed and cosmetic industry.

Vitaplant offers a wide range of services around research, development and production:

- Selection and breeding programs of innovative plant varieties to find the optimal plant for medicinal use
- Assurance of quantity of active compounds and plant purity (e.g. pesticides, micro-biological contamination)
- Pilot cultivation to ensure scalability of production
- Standardized, controlled cultivation under Good Agricultural and Collection Practice (GACP)
- Registration of European plant variety rights

With more than 20 years of experience and projects with numerous plant species, Vitaplant has developed a strong expertise in herbal raw material research and supply. This is complemented by modern infrastructure at the Vitaplant head offices in Uttwil, including computer controlled greenhouses, a field trial station of 60,000 m<sup>2</sup> and a GMP-certified raw material warehouse. Vitaplant works with a worldwide network of professional partners and has its own subsidiaries in strategic geographical areas. With this, Vitaplant is able to reliably provide complete, tailor-made agro solutions from just one source.



## THE ZELLER DIFFERENCE

### FROM SEED TO PATIENT

#### SPECIAL EXTRACT

We guarantee unique, high quality extracts processed from selected and controlled plants. The optimal ingredient spectrum is extracted from each plant.

#### CONSISTENCY

We ensure batch-to-batch consistency to maintain the highest quality standards of our phyto-pharmaceuticals.

#### CLINICALLY PROVEN

The results of our clinical trials have been published in numerous international peer-reviewed scientific journals, such as the British Medical Journal and Journal of Allergy and Clinical Immunology.

#### HIGHLY EFFECTIVE

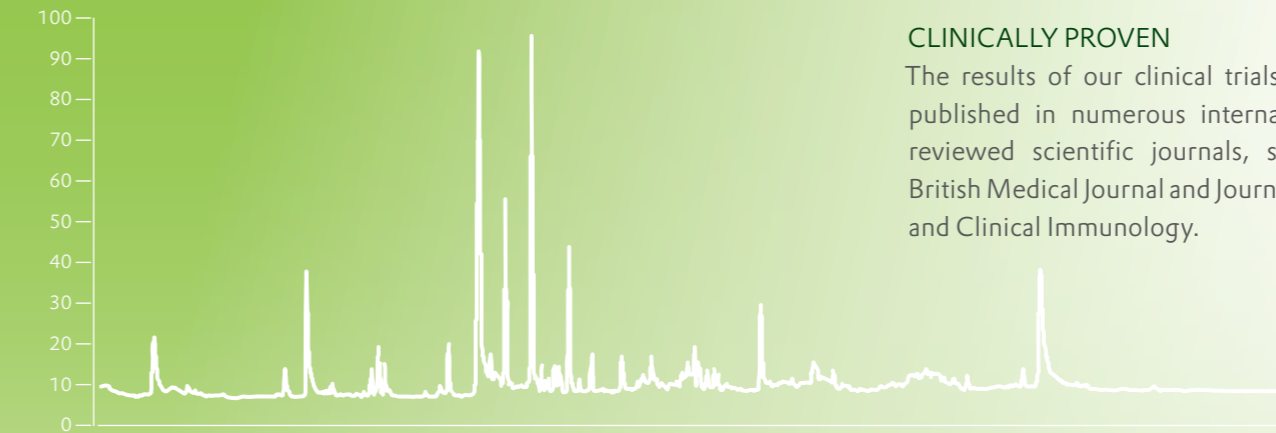
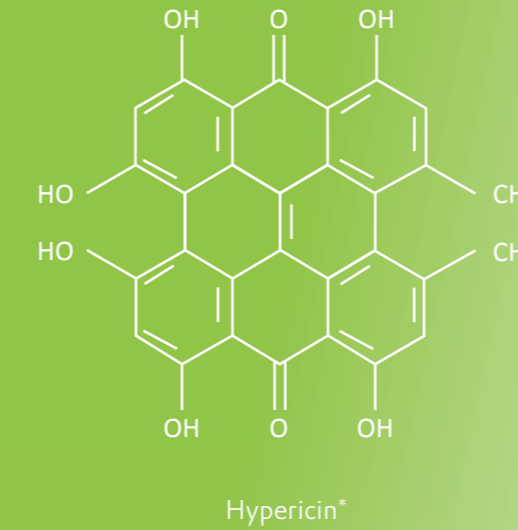
Our products are non-inferior to chemical synthetic drugs in head-to-head trials and are the preferred choice in first-line treatment among healthcare professionals.

#### EXCELLENT SAFETY

Our products have an excellent safety profile, which makes them suitable for long-term therapy.

#### SWISS MADE

All our products are manufactured in Switzerland and are leading the domestic phyto-pharmaceutical market.



\*Hypericin; active component of Ze 117

# ZELLER INTERNATIONAL PORTFOLIO

Category	Indication	Trademark*	Extract
<b>CNS</b>	Sleep Disorders	<b>Redormin®</b>	Valerian and hop dry extract Ze 91019
	Depression	<b>Remotiv®</b>	St. John's wort dry extract Ze 117
<b>Gynecology</b>	PMS	<b>Prefemin®</b>	Agnus castus dry extract Ze 440
	Menopause	<b>Cimidona®</b>	Black cohosh dry extract Ze 450
<b>Allergy</b>	Allergic Rhinitis	<b>Tesalin®</b>	Petasites hybridus extract Ze 339

Our products are available in more than 25 countries around the world. Some of them belong to the "Well-Established Use" category of the HMPC monograph published by the European Medicine Agency. These products are the best in their class.

We continuously support our partners with professional product documentation (dossiers in CTD format), scientific material, training sessions and product life cycle management.



## ZE 339 TESALIN®

"New herbal entity", no similar product worldwide

Dual mode of action: anti-allergic and anti-inflammatory effect

Head-to-head studies against cetirizine, fexofenadine and desloratadine

Does not cause fatigue<sup>1</sup>



**Extract** *Petasites hybridus* leaf extract Ze 339

**Indication** Treatment of allergic rhinitis (hay-fever) and related symptoms of the eyes, nose and throat

**Formulation** Film coated tablets standardized to 8 mg petasins



### CLINICAL STUDIES\*

Publication	Study Design	Results
<b>Schapowal, et al.</b> Phytotherapy Res. (2005)	Prospective, randomized, double-blind, parallel group comparison study	Ze 339 and fexofenadine are comparably efficacious in improving symptoms of intermittent allergic rhinitis
<b>Schapowal, et al.</b> Arch Otolaryngol Head Neck Surg. (2004)	Prospective, randomized, double-blind, placebo controlled, parallel group comparison study	Significant dose dependence of efficacy but no change in the incidence of adverse events
<b>Schapowal, et al.</b> BMJ (2002)	Randomized, double blind, parallel group comparison study	Improvement of symptoms of intermittent allergic rhinitis is similar for Ze 339 and cetirizine

## ZE 440 PREFEMIN®

N°1 treatment of PMS in Switzerland

"Well-established use" by HMPC of EMA

Causal treatment instead of symptom alleviation as with analgesics or SSRIs

Effective for physical and mental symptoms of PMS



**Extract** *Agnus castus* dry extract  
Ze 440

**Indication** Treatment of premenstrual syndrome (PMS) and menstrual cycle disorders

**Formulation** Film coated tablets containing 20 mg Ze 440



### CLINICAL STUDIES\*

Publication	Study Design	Results
<b>Eltbogen, R. et al.</b> Journal für Gynäkologische Endokrinologie (2015)	Observational study	Efficacious in treatment of menstrual cycle irregularities, polymenorrhoea, oligomenorrhoea and amenorrhoea
<b>Schellenberg, R. et al.</b> Phytomedicine (2012)	Double blind, randomized, placebo controlled study	Dose dependent efficacy in relieving symptoms of PMS (Efficacious when applied in a dose of 20 mg per day)
<b>Schellenberg, R. et al.</b> British Medical Journal (2001)	Prospective randomized, double-blind, parallel grouped controlled study	Significant superiority of active treatment in women with PMS, well tolerated
<b>Berger, D. et al.</b> Arch Gynecol Obstet (2000)	Prospective, open, multicentre study	Effective regarding improvement of PMS symptoms

\* selection of clinical studies for Ze 440; further studies upon request

## ZE 450 CIMIDONA®

N°1 treatment of menopausal disorders in Switzerland

No hormonal effect

Good safety record, over 195 million sold DDD (2017)

No clinically relevant drug-drug interactions reported



**Extract** *Cimicifuga racemosa* dry extract Ze 450

**Indication** Treatment of menopausal disorders with symptoms such as hot flushes, sweating, sleep disorders, nervousness and depressive moods

**Formulation** Tablets containing 6.5 mg or 13 mg Ze 450



### CLINICAL STUDIES\*

Publication	Study Design	Results
<b>Drewe, J. et al.</b> Phytomedicine (2013)	Observational study	3-months treatment with 13 mg decreased symptoms significantly (total KMI); continuation of treatment with 13 or 6.5 mg decreased symptoms further
<b>Schellenberg, R. et al.</b> Evidence-Based Complementary and Alternative Medicine (2012)	Multicentre, randomized, double-blind, placebo controlled, parallel group study	Treatment with Ze 450 was confirmed as efficacious (MRS II); well tolerated
<b>Lopatka, L. et al.</b> Journal für Menopause (2007)	Observational study	Treatment with Ze 450 was confirmed as efficacious (MRS II); well tolerated

\* selection of clinical studies for Ze 450; further studies upon request

# ZE 117 REMOTIV®

Clinically proven superiority vs. placebo and non-inferiority vs. fluoxetine and imipramine

"First-line" treatment of mild to moderate depressive episodes

Very low potential for drug-drug interactions due to low hyperforin content<sup>1,2</sup>

Excellent safety profile



**Extract** St. John's wort dry extract Ze 117

**Indication** Treatment of mild to moderate depressive episodes according to WHO ICD-10 F32.0/F.32.1

**Formulation** Film coated tablets containing 250 mg or 500 mg Ze 117



## CLINICAL STUDIES\*

Publication	Study Design	Results
<b>Brattström, A. et al.</b> Phytomedicine (2009)	Open, multicentre safety study	Ze 117 is a safe and effective way to treat mild to moderate depression over long periods of time (1 year)
<b>Woelk, H.</b> British Medical Journal (2000)	Prospective, randomized, double-blind, parallel group controlled trial	Ze 117 is equivalent to imipramine in treating mild to moderate depression and better tolerated
<b>Schrader, E. et al.</b> Int Clin Psychopharmacol (2000)	Prospective randomized, double-blind, parallel grouped controlled study	Ze 117 hypericum extract is equipotent to fluoxetine, Ze 117 with significantly less side effects
<b>Schrader, E. et al.</b> Human Psychopharmacol (1998)	Prospective, double-blind, randomized, placebo-controlled, multicentre study HAMD-21, CGI, VAS	Significant difference between Ze 117 and Placebo. 56 % responders compared to 15 % in placebo group after 6 weeks of treatment

<sup>1</sup> Will-Shahab, L. et al. Eur J Clin Pharmacol (2009)  
<sup>2</sup> Müller, SC. et al. Clin Pharmacol Ther (2004)

\* selection of clinical studies for Ze 117; further studies upon request

# ZE 91019 REDORMIN®

Dual mode of action (acts via adenosine and melatonin receptors)

Reduces significantly the sleep latency as well as the total wake time per night and improves the sleep architecture

Does not cause drowsiness or morning hang-over



**Extract** Fixed combination of valerian and hop dry extract Ze 91019

**Indication** Treatment of sleep disorders such as difficulties in falling asleep, staying asleep as well as restless sleep

**Formulation** Film coated tablets containing 250 mg valerian and 60 mg hop or 500 mg valerian and 120 mg hop



## CLINICAL STUDIES\*

Publication	Study Design	Results
<b>Koetter, U. et al.</b> Phytotherapy research (2007)	Randomized, double blind, placebo-controlled, prospective	Significantly superior to placebo in reducing sleep latency
<b>Schellenberg, R. et al.</b> Planta Med (2004)	Randomised, placebo-controlled clinical pharmacology study	The valerian-hops extract Ze 91019 acts via a central adenosine mechanism in healthy male volunteers
<b>Rodenbeck, A. et al.</b> Somnologie (1998)	Randomized, double-blind, placebo-controlled, parallel group comparison	Supports the use of valerian-hops for the improvement of subjective sleep quality in mild, non-chronic insomnia
<b>Flesch, P.</b> Geriatric Praxis. (1997)	Open, parallel group polysomnographic comparison study	Improvement of hypnograms after discontinuation of chronic benzodiazepine use substituted by Ze 91019

\* selection of clinical studies for Ze 91019; further studies upon request