Message from the Chairman Dr. Friedrich-Wilhelm Kuehne

To whom it may concern:

Nothing is set in stone when it comes to clinical research, but occasionally we will have to reinvent the wheel. Victor Hugo ones stated: *"Nothing is more powerful than an idea for which the time had come."*

OXOVASIN (Drug substance: TCDO) has been just approved by the Food and Drug Administration (FDA) of Thailand, the first shipment arrived in Bangkok on 16th June 2023.

OXOVASIN is a clinically proven, safe, and effective topical solution for treatment of infected, inflamed, chronic and immune compromised wounds, burns, decubitus, and wound cavities, **based on unique modulation of the innate immune response**:

1. **OXOVASIN effectively terminates cell- and tissue destruction** via specific inhibition of the Myeloperoxidase (MPO)-pathway.
2. **OXOVASIN creates superior tissue repair by inducing apoptosis, phagocytosis, and neo-angiogenesis.** It modulates the Phosphatidyl-Inositol-Kinase (PI3K)-pathway.
3. **OXOVASIN-derived efficient removal of apoptotic cells is 'sine qua non' for tissue development and homeostasis, as well as protection against neoplasia and chronic inflammation.**
4. **OXOVASIN is pharmacologically effective in treatment of wounds in patients with immune suppression and anergic wounds** by reversing the effects of cortisone. (see: In Memoriam: Paul Ehrlich).

OXOVASIN is identical with the international known drug Oxoferin which is manufactured by the same factory at OXO Translational Science Inc., Wanzleben, Germany.

OXO Translational Science Inc. is the leading company in development of chlorite-based drugs.

In Memoriam Prof. Paul Ehrlich, Shriners Burn Institute, Boston, USA

In 1990 I had the honor to host the '**International Symposium for Tissue Repair'** in Pattaya, Thailand.

It was organized by **Prof. Nopadol Wora-Urai**, Phramongkutklao Military Hospital, Bangkok, **Prof. Thong-Ueb Uttaravichien** and **Assoc. Prof., Vajarabhongsa Bhudhisawasdi**, both from Srinagarind University Hospital, Khon Kaen, Thailand.

Among the 200 attendees from Asia, USA, Europe, including Russia (Chernobyl), were world-renowned scientist involved in pre- and clinical research of wound healing and tissue repair. The most prominent among the attendees were **Prof. Thomas K. Hunt** from San Francisco University Hospital (UCSF). Owing to his experiences as a physician in the Vietnam War, he dedicated his academic life to improve and teach knowledge about tissue repair. **Prof. Charles Baxter** from University of Texas, Dallas, who tried to save President John F. Kennedy's life after he was shot in his open limousine, presented his scientific legacy 'Nutrition in Burns'.

Placed for eternity was the presentation from **Prof. Paul Ehrlich**, great grandson of the Nobel Laureate Paul Ehrlich. He worked at Shriners Burns Hospital, Boston, USA.

Paul developed an experimental animal model (in 1990) to test efficacy and safety of drugs with the objective to induce apoptosis/phagocytosis, and homeostasis in impaired wound healing of immunocompromised subjects, an unmet medical need. Together with **Prof. Ludwig Hatz** (Ludwig's Maximilian University (LMU) Munich, Germany) he published their findings in **Springer's 'Phagocytic Biology'**: "TCDO reversed the effect of Cortisone on wound healing. Treatment with TCDO resulting in statistically significantly accelerated wound healing of immune-compromised wounds". Animals receiving cortisone in combination with TCDO displayed markedly enhanced wound healing, including restoration of tensile strength, collagen synthesis, and wound contraction. The results indicate that TCDO could be a potential agent of wound healing in immunosuppressed patients and anergic wounds.

Other Topics of the named conference were 'Oxygen as an antibiotic', and 'Modulation of Innate Immune Response by Oxidants with anti-inflammatory properties. Pharmacological approaches to limit Cell- and Tissue Damage were discussed, data from Pre- and Clinical studies using the chlorite-based drug TCDO were presented revealing robust clinical efficacy in treatment of epithelial dysfunction in Proctitis (**Prof. Thong-Ueb Uttaraviechien**) and hemorrhagic/interstitial Cystitis (**Assoc. Prof. Vutisiri Veerasarn**, Siriraj Hospital, Bangkok, and **Assoc. Prof. Vicharn Lorvidhaya**, Chiang Mai University, Chiang Mai) and Mucositis (Radio-Oncology Group of Thailand).

Prof. Erich Elstner and Prof. Schempf from Klinikum Rechts der Isar/ Technical University of Munich (TUM) Munich, Germany (the Oxygen Guru) presented molecular mechanism of the chlorite molecule with **Hemeproteins**, among it the **specific inhibition of Myeloperoxidase** (MPO), **leading to effective resolution of neutrophilic inflammation by induction of apoptosis/phagocytosis. Efficient removal of apoptotic cells is necessary for tissue development and homeostasis, as well as protection against neoplasia and chronic inflammation.**

Assoc. Prof. Chairat Burusapat and Sophilak Sringkarawat (Phramongkutklao Military Hospital, Bangkok),

Thirty (30 years) later (2021), they published in 'Plastic and Reconstruction Surgery' the results from a Prospective, Randomized, Controlled Trial (RCT), comparing **N**egative-**P**ressure **W**ound **T**herapy (**NPWT**) with NPWT and installation of TCDO (abbreviated **NPWTi**). The results reported included a blinded analysis from an independent pathologist analyzing the quality of deep tissue after 15 days NPWTi and NPWT alone treatment. The highlights were:

1. **Bacteriology: No difference in microbiome reduction in both groups**
2. **Healing: Statistically Significantly better wound healing in NPWTi compared to NPWT alone (p>0.01 on day 15)**
3. **Granulation in NPWTi was superior compared to NPWT alone**
4. **Tissue quality: NPWTi did not leave any edematous stroma cells behind, and showed visible neo-angiogenesis,**
5. **NPWT alone left substantial edematous stroma cells behind, and no neo-angiogenesis was detected (see histology)**

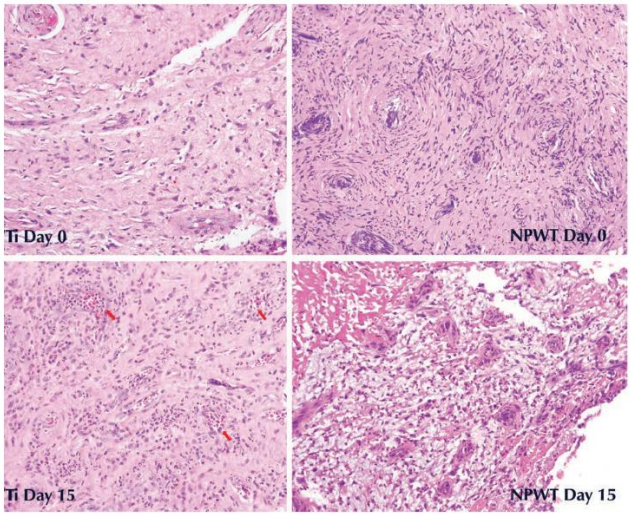

Figure: *Comparison of the histopathologic results on days 0 and 15 between the NPWTi and NPWT-alone groups (hematoxylin and eosin staining; original magnification, ×100). Microscopic examination showed granulation tissue characterized by markedly proliferating capillary-size blood vessels with stromal cells and moderate infiltration of lymphocytes, plasma cells, and neutrophils in both the NPWTi and NPWT-alone groups. However, the NPWT-alone group was found to have more edematous stromal cells and less neoangiogenesis than the NPWTi group (red arrow demonstrates new capillary-size blood vessels).*

Image source: Burusapat-Sringkarawat, Plastic and Reconstructive Surgery 148(2):p 339-352, August 2021.

Unfortunately, the investigators did not enroll immune-compromised patients out of 107 patients selected for study entry, despite referencing to Paul Ehrlich's work and results of other investigators.

I tried to contact Paul Ehrlich to debate this paper with him, only to find out that he passed away during the Corona Pandemic with only 79 years of age.

Paul as a believing Catholic lived a modest way. His legacy is still alive.

Burasapat and colleagues confirmed prior findings from their German colleague **Prof. Ulf Thiede** (**Zenker, Erdmann, Thiede**, University of Kiel, Germany).

1. TCDO installation statistically significantly accelerated wound healing but did not show difference in microbial reduction.

2. TCDO installation showed visible granulation on bones, tendon, and facies, statistically significantly accelerated wound healing as well as excellent deep tissue quality, compared to antiseptic solutions (Betaisodona).

Conclusion: Pharmacological Control of Cell and Tissue Destruction, paired with induction of apoptosis and phagocytosis by OXOVASIN installation, is an ultimate approach for state-of-the-art wound healing and tissue repair.

It is also an ultimate approach for treatment of chronic inflammation.

Assoc. Prof. Narongchai Yingsakmonkol is also member of the **Srinagarind University Hospital, Faculty of Medicine, Khon Kaen**. He was once awarded a scholarship to Heidelberg University, Department of Surgery (**Prof. Herfarth and Prof. Buechler**) and taught for years at **Srinakharinwirot University**, Nakhon Nayok, Thailand. He dedicated his life to wound healing and tissue repair, in a similar fashion as T.K. Hunt from San Francisco, and he became one of the most experienced Surgeons in treatment of complicated wounds in ASEAN, including diabetic osteomyelitis. His published results were outstanding and were just confirmed by **Prof. Yazid Bajuri** from National University of Malaysia, Kuala Lumpur. After retirement from the academic school, he still treats complicated wounds at Private Hospitals (Ladprao Hospital and Kasemrat Hospital).

I bow my head in recognition to all of those mentioned above for their valuable contributions to pre-and clinical science.

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