# Seborrheic Keratosis Removal in Multi-Center Phase I/II Trial Using a Novel Topical Formulation (BL-5010)

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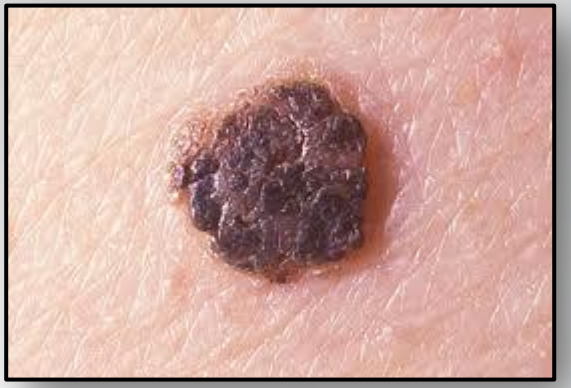
# Introduction: Seborrheic Keratosis



- The most common non-cancerous skin lesions of the older age
- Appears in various colors, forms and sizes
- Often patients present with multiple lesions, generally asymptomatic but occasionally irritation or trauma may occur with itching, pain and bleeding
- Develop from the basal cell layer of the epidermis and migrate towards the surface of the skin where they die and make a keratin layer that acts as a protective layer for the skin
- Treatments (mostly for cosmetic reasons) include cryosurgery, laser therapy, curettage or electro-cautery, which are painful and often result in local bleeding, infection, blistering, and hematoma and do not provide a solution for removal of large numbers of lesions in the same patient

# BL-5010: Preclinical Activities

- Mode of Action
  - Non-surgical removal of the skin lesion by a caustic cell burn, due to a low pH
  - Non-specific crosslinking of cellular proteins leading to cell death, fixation and mummification of the tissues

- Animal Studies (GLP certified facility accordance with CHMP guidelines):
  - A single dose dermal tolerance study in minipigs
  - A sensitization study in guinea pigs
  - Minimal skin injury - consistent with the intended clinical use
  - Hair growth observed within the treated skin area suggests that the injury is reversible
  - BL-5010 is not a contact sensitizer, suggesting no additional safety concerns on repeated administration

- Based on the MoA and safety results, BL-5010 has been classified as a Medical Device in Europe

# Phase I/II Clinical Trial

## Open-label, single-arm, single application, safety and efficacy study

- 60 SK patients were recruited for a single application
- Patients were treated and followed-up for 6 months
- Clinical sites: Germany and the Netherlands
- Endpoints:
  - Primary: Physical examinations, adverse events, and vital signs (pulse and blood pressure)
  - Secondary:
    - Assessments of dermal irritation (erythema, edema formation) at the site of application
    - Investigator-assessed clinical lesion response post treatment
    - Investigator-assessed and patient-assessed cosmetic outcomes at the site of the index lesion
    - Proportion of patients who provide index lesion adequate for pathological assessments

**Clinical Lesion Response Categorical Scale**

| Response | Assessment |
|---|---|
| Complete | Complete disappearance of “index lesion” |
| Partial | Reduction in “index lesion” ≥25% and <100% |
| None | <25% reduction or an increase in size of the “index lesion” |

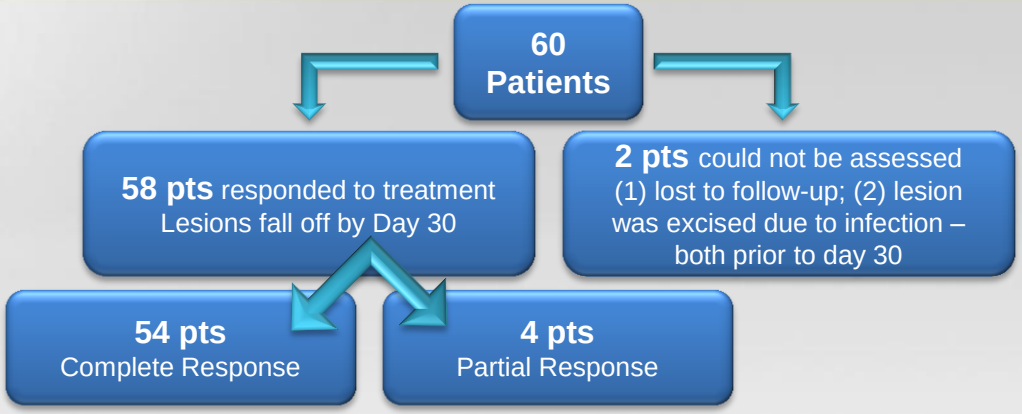
**Clinical Lesion Response Categorical Scale**

| Outcome | Investigator/Patient Cosmetic Assessments Categories |
|---|---|
| Excellent | No scarring, atrophy, or induration, slight or no redness or change in pigmentation compared with adjacent skin |
| Good | No scarring, atrophy, or induration, moderate redness or increase in pigmentation compared with adjacent skin |
| Fair | Slight to moderate occurrence of scarring, atrophy, or induration |
| Poor | Extensive occurrence of scarring, atrophy, or induration |

## BL-5010 was Applied via a Wooden Stick

- Dermatologists pressed the wooden stick onto lesion to cover its whole surface, both perpendicularly (at a 90° angle) and circularly at a 45° angle
- The procedure was repeated on all aspects of the lesion until it softened and completely flattened
- Each process lasted few minutes

# Clinical Trial Results




## Efficacy

### I. Lesion removal

>96% of the patients (58/60) by day 30

### II. Cosmetic outcome

94.6% of investigator and 84% of patient-assessed cosmetic outcomes were good or excellent 180 days following treatment

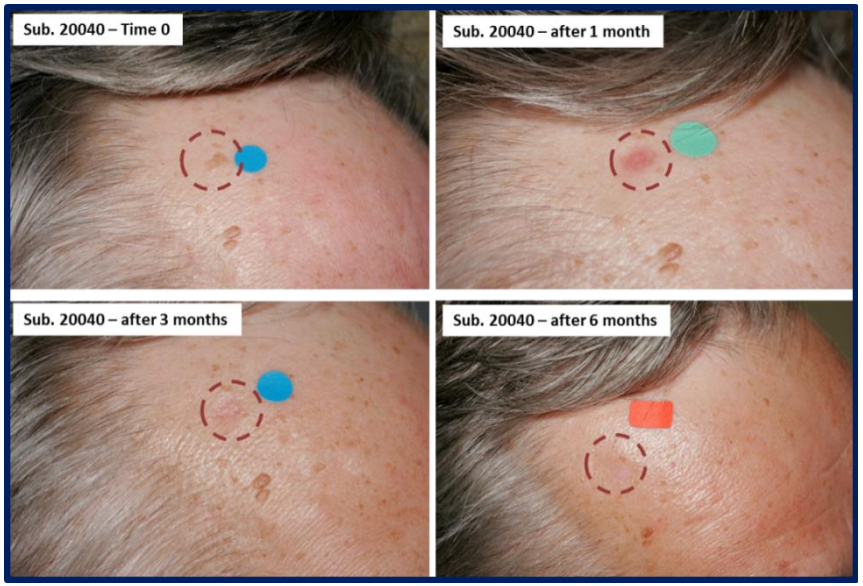
### III. Lesion preservation for further analysis

BL-5010 allows lesion preservation following detachment, for subsequent histopathological diagnosis

## Safety

**BL-5010 was safe and well tolerated with no persistent or irreversible adverse effects at all treated sites**

| Adverse Event | n=60 | | | | | |
|---|---|---|---|---|---|---|
| | Mild | | Moderate | | Severe | |
| | n | % | n | % | n | % |
| One or more drug-related AEs | 6 | 10 | 0 | 0.0 | 0 | 0.0 |
| | | | | | | |
| **General Disorders and Administration Site** | **2** | **3.3** | **0** | **0.0** | **0** | **0.0** |
| *Feeling hot* | 1 | 1.7 | 0 | 0.0 | 0 | 0.0 |
| *Secretion discharge* | 1 | 1.7 | 0 | 0.0 | 0 | 0.0 |
| **Infections and Infestations** | **1** | **1.7** | **0** | **0.0** | **0** | **0.0** |
| *Wound infection* | 1 | 1.7 | 0 | 0.0 | 0 | 0.0 |
| **Nervous System Disorders** | **1** | **1.7** | **0** | **0.0** | **0** | **0.0** |
| *Burning sensation* | 1 | 1.7 | 0 | 0.0 | 0 | 0.0 |
| **Skin and Subcutaneous Tissue Disorders** | **5** | **8.3** | **0** | **0.0** | **0** | **0.0** |
| *Pruritus* | 4 | 6.7 | 0 | 0.0 | 0 | 0.0 |
| *Scab* | 1 | 1.7 | 0 | 0.0 | 0 | 0.0 |
| *Skin hyperpigmentation* | 1 | 1.7 | 0 | 0.0 | 0 | 0.0 |



# Summary and Conclusions

- A single application of BL-5010 was safe and resulted in detachment of the Seborrheic Keratosis (SK) lesion from the skin with no serious accompanying complications
- BL-5010 presented a superb and complete SK removal rate of 96.7%
- BL-5010 obtained very good cosmetic outcome according to patients and dermatologists
- Easily, safely and accurately applied on lesions with minimal training required
- Highly versatile and could potentially be extended to treat various indications such as actinic keratosis, skin tags and warts
- BL-5010 may be considered as an alternative treatment to painful, invasive and expensive therapy

# Conflict of Interest

Study was sponsored by BioLineRx Ltd

- **Dr. Etgar Levy-Nissenbaum** – BioLineRx's employee
- **Prof. Hok Bing Thio** – was investigator in this clinical trial
- **Dr. Pinchas Burstein** – the inventor of BL-5010 and BioLineRx's consultant
- **Prof. Diamant Thaçi** – was investigator in this clinical trial