A MARKOV MODEL TO DETERMINE THE COST-EFFECTIVENESS OF A MULTI-TARGETING BACTERIAL GENE THERAPY (AUP-16) AT HEALING A DIABETIC FOOT ULCER COMPARED TO THE CURRENT STANDARD OF CARE

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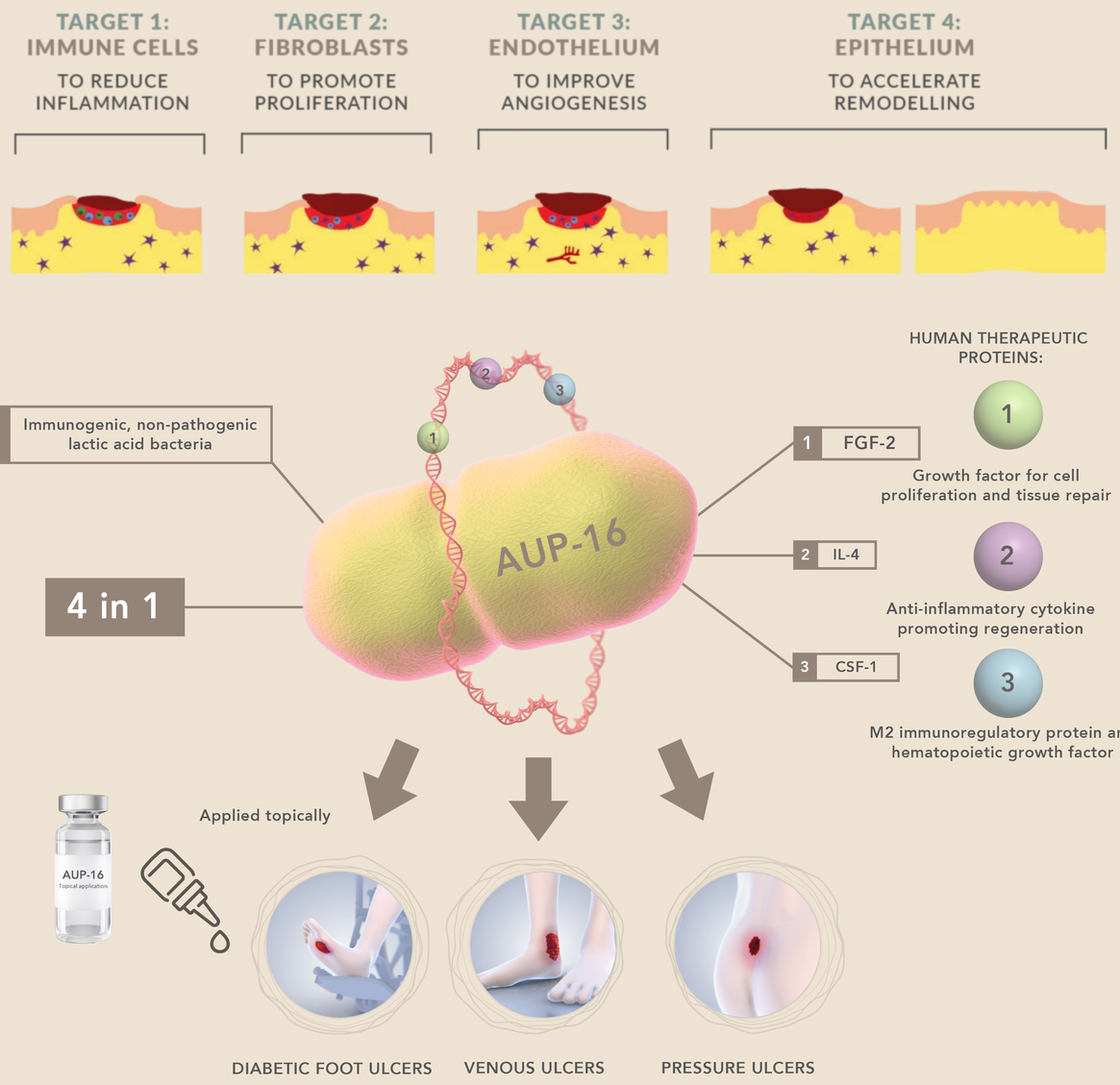
INTRODUCTION

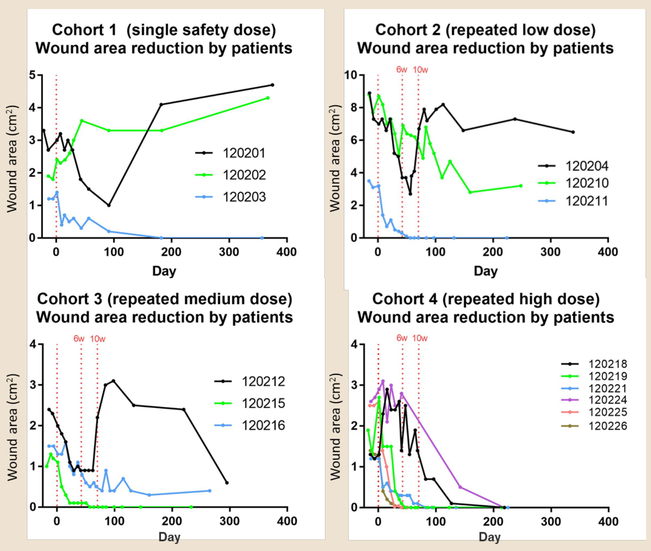
DIABETIC FOOT ULCERS (DFUs): a serious complication of Diabetes, affecting 19-34% of diabetic patients, leading to amputation, hospitalization, death. DFUs reduce quality of life, increase mortality rates: 20% of people with DFUs will require amputation, 50% of amputees will die within 5 years.
BURDEN & COST: Massive burden on healthcare resources. Europe: €10,091 yearly cost per DFU patient (hospitalization being the major cost). USA: $9-13 billion/year for DFU management, $11,710-$16,833 yearly cost per patient.
STANDARD OF CARE (SOC): Surgical debridement, infection control, moist-wound care, off-loading footwear if needed. Advanced treatments include negative wound pressure, skin substitutes, grafts, and topical growth factors. Most SOC and adanced DFU treatments are medical devices.
GOAL of this study: determine if a new Multi-Targeting Bacterial Gene therapy (AUP-16), is more cost-effective than SOC at healing a DFU.

AUP-16 FOR CHRONIC WOUNDS
DIABETIC FOOT ULCER

MODE OF ACTION



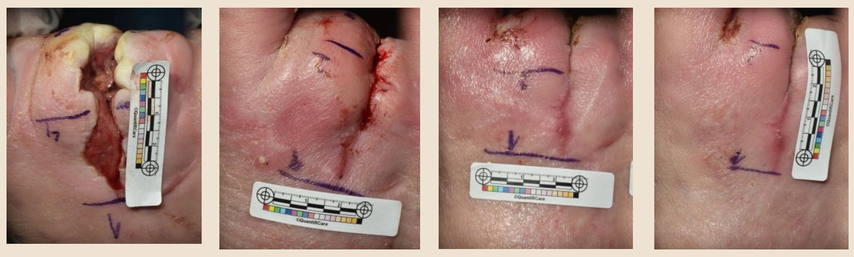
PHASE 1 STUDY OUTCOME



Best in class efficacy:

- 83% of the patients who received the lead therapeutic dose reached **complete healing.**
- >30% **wound size reduction** in first 2 weeks of treatment vs. >17% wound size increase in 2 weeks run-in period with SOC
- Median **time to heal**: 9.2 weeks / 65 days.
- **No recurrence** of healed wounds after 12 months follow-up.
- **No Dose Limiting Toxicity,** no systemic or local safety nor tolerability issues.

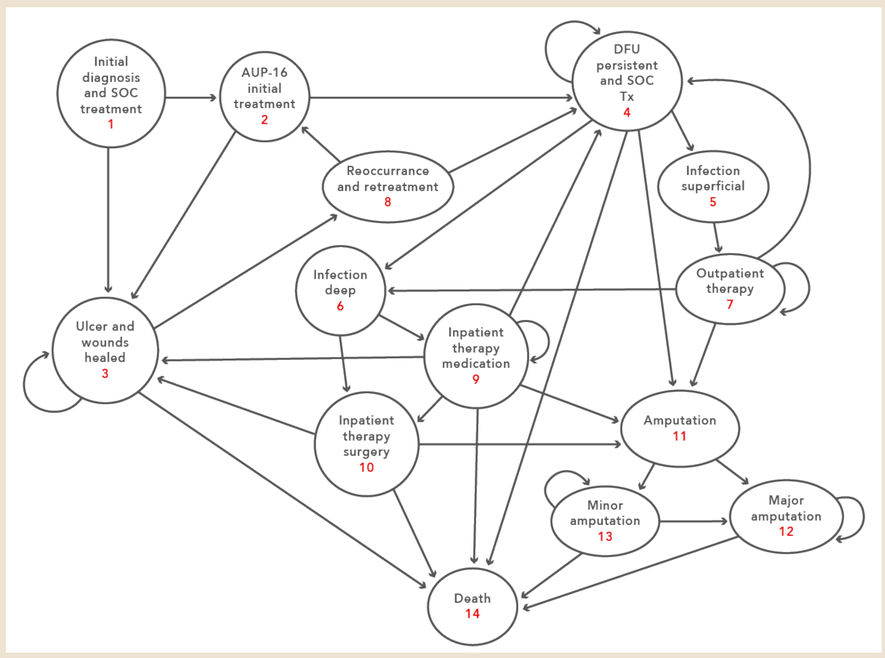
EXAMPLE: Cohort 2, low dose, 3 times per week for 6 weeks



Before treatment Wound 10 weeks old | End of treatment 6 weeks | 2 weeks after end of treatment | 4 weeks after end of treatment

METHODOLOGY

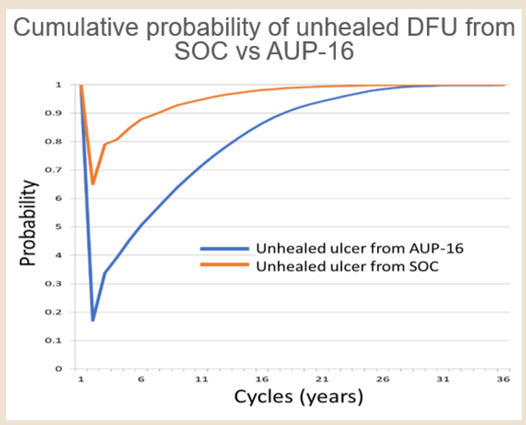
A MARKOV MODEL was used to compare AUP-16 and SOC at outcomes including QALY's, costs, DFU healing, reoccurrence, death, infections, and amputation. Costs were from the **US MEDICARE** perspective.



- Transition probabilities, rates of amputation, infection, recurrence, death, and QOL scores using **EUROQOL** were from published literature.
- AUP-16 efficacy rates were from the company's Phase 1 trial.
- **Cost-Utility Analysis (CUA)** methodology was used to determine cost-effectiveness of AUP-16 compared to SOC.
- MEDICARE costs, number of quality adjusted life-years, were determined for each of AUP-16 and SOC.
- **Incremental Cost-Effectiveness Ratio (ICER)** was determined as follows: **ICER = [Cost (AUP-16) – Cost (SOC)] / [Quality-life years (AUP-16) – Quality-life years (SOC)]**
- AUP-16 ICER is compared **Willingness To Pay (WTP)**
- In US, WTP of $100,000-$150,000 is considered acceptable.

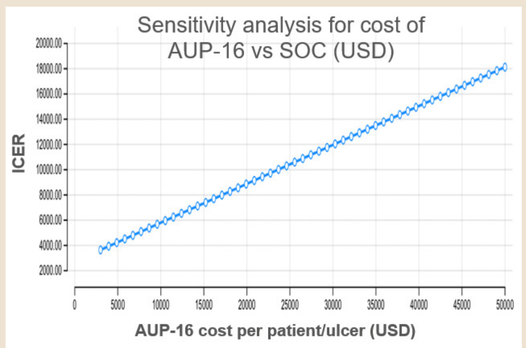
RESULTS

- AUP-16 is cost-effective vs. standard of care. (SOC) for DFUs, with an **ICER of $3,909/QALY**
- Even at higher prices, AUP-16 remains cost-effective.
- In sensitivity analyses, the ICER ranges **$1 to $7,434 per QALY.** AUP-16 is never cost-dominant over SOC.



CONCLUSION

- **AUP-16 IS MORE COST-EFFECTIVE THAN STANDARD OF CARE** at healing DFUs
- Baseline ICER: **$3,909/QALY.**
- The model is robust to a comprehensive sensitivity analysis, with the ICER never exceeding $100,000/QALY.



KEY LIMITATIONS

- Cycles of 1 year were used, while patients may change state in shorter time. However, the information used provided cost of a state for 12 months.
- It was assumed that Medicare would reimburse the costs of AUP-16.
- Charges and costs from studies in literature conducted over a variety of years were not recalculated or discounted to a specific index year.
- Healing and reoccurrence rates for AUP-16 are based on the company Phase-1 study. Results of ongoing larger Phase-2 study may differ.