Clinical Experience with the MicronJet600® - from vaccines to immunotherapy and beyond

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NanoPass Background

• Founded in 2000
• Core technology - microneedle device for ID delivery - MicronJet600®
• Already approved for marketing in the USA, Canada, Europe, Hong-Kong, Korea, China, Brazil
  o For substances approved for delivery into the skin
• Multiple clinical trials data:
  o Multiple vaccines
    ➢ Influenza (Seasonal, h1n1, H5)
    ➢ Zoster, Polio, PPD
  o Immunotherapy
    ➢ Allergy
    ➢ Cancer
    ➢ T1 Diabetes
Vaccines:
- Improved Immunogenicity vs IM / SC
  - Proven in a Ph. II study with flu vaccine (Sanofi Fluzone® ID)
  - Proven in a Ph. I study with zoster vaccine (Merck)
- Dose Sparing
  - 5x-27x dose sparing across multiple vaccines (Ph. I, II)
  - Benefits include COGs reduction (x5) and increased capacity
- Adjuvant Sparing
  - Proven in Ph. I collaborative Big Pharma study
  - Critical in pediatrics where adjuvants are considered unsafe (US)

Immunotherapy:
- Cancer and Allergy immunotherapy
- Autoimmune diseases (T1DM, MS?)

Systemic Delivery:
- Insulin – improved kinetic (proven by NP)
First silicon needle ever registered with FDA

- Unique shape and process using MEMS technology
- Microneedles are barely visible to the naked eye

Innovative Design:
  - Pure silicon single crystal
  - Thick-walled pyramid design

Off-set channel design:
  - Does not clog or leak

Sharp tip reduces penetration forces
Proven **safety, efficacy** and **usability** in multiple clinical trials
<table>
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<tr>
<th>Field</th>
<th>Phase</th>
<th>Device used</th>
<th>N</th>
<th>Benefit demonstrated</th>
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<td>Painlessness</td>
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Clinical evaluation of a novel microneedle device for intradermal delivery of an influenza vaccine: Are all delivery methods the same?☆

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MicronJet Superiority Over Mantoux

- 280 healthy adult volunteers; Inflexal® V (Crucell)

MicronJet injections (Group C, 3 µg) yielded higher immunogenicity than other ID groups using Mantoux (Groups A1, A2, and A3) and the IM group (Group B)

Immune response and reactogenicity of intradermal administration versus subcutaneous administration of varicella-zoster virus vaccine: an exploratory, randomised, partly blinded trial

Chan R Beals, Radha A Railkar, Andrea K Schaeffer, Yotam Levin, Efrat Kochba, Brian K Meyer, Robert K Evans, Eric A Sheldon, Kenneth Lasseter, Nancy Lang, Adriana Weinberg, Jennifer Canniff, Myron J Levin

Published Online: 06 April 2016
Immunogenicity Results: gpELISA and IFN-gamma ELISPOT

224% and 145% increase in full and 1/3 dose ID respectively vs. 74% and 64% in full and 1/3 dose SC. Error bars represent 90% Confidence Intervals;
ID Zostavax study – CMI Data

- VZV-specific CD4+ memory cells (CD4+ CD69+ CD27+ CD28+ CD45RO+) were significantly higher at 6w than at BL for ID.
  - Mean change: -8.17% SC vs. +0.16% ID (p=0.0449).

- The proportion of VZV-specific CD4+ effector memory cells also approached statistical significance.
  - Mean change: -0.87% SC vs +1.06% ID (p=0.0954).

- Improvements in CMI with ID administration of the Zostavax may be confirmed in a larger sample.
Preference Data (N=267)

Subject preference for future vaccines
- MicronJet600™: 3%
- Ordinary Hollow Steel Needle: 15%
- No Preference: 82%

Subject preference for their children for future vaccines
- MicronJet600™: 11%
- Ordinary Hollow Steel Needle: 5%
- No Preference: 77%
- Not Applicable: 7%

Pain with MJ600™ Injections
- Painless: 76%
- Painful But Less Than Ordinary Hollow Steel Needles: 19%
- Painful As Much As Ordinary Hollow Steel Needles: 2%
- More Painful Than Ordinary Hollow Steel Needles: 3%

Intimidation with MJ600™ injections
- Not Intimidating: 68%
- As Intimidating As An Ordinary Hollow Steel Needle: 28%
- Less Intimidating Than An Ordinary Hollow Steel Needle: 3%
- More Intimidating Than An Ordinary Hollow Steel Needle: 1%
The Future of ID Delivery of Vaccines and Immunotherapeutics

• Launch products in proven indications (flu, live attenuated vaccines, rabies, iPV)
• Improve vaccine efficacy and safety in “challenging” populations
  o Elderly, pediatric and the immunocompromised
• Use ID delivery for immunotherapeutics:
  o Allergy
  o Cancer
  o Type I diabetes and other autoimmune diseases
Allergy Immunotherapy

• The allergy field is moving from crude allergen treatments (desensitization), which has been the mainstay for 90 years, to 2\textsuperscript{nd} generation therapies (sub lingual drops/tablets), which gained limited acceptance due to limited efficacy and challenging compliance

• 3\textsuperscript{rd} generation products are developed by biotech companies to achieve a long-lasting curative effect. These products are using ID delivery

• NanoPass supports over a dozen (concluded and on-going) Phase II or III clinical trials
• Science Magazine named “cancer immunotherapy” as the 2013 breakthrough of the year

• ID delivery is being evaluated for improving cancer vaccines (>50 ID agents in development)

• NanoPass supports several phase I-II cancer vaccines clinical trials
Summary

- Microneedle ID delivery has demonstrated significant dose sparing and improved immunogenicity in phase I-III clinical trials, mostly in prophylactic vaccination.
- The world is moving towards harnessing the skin’s potent immunity to bolster immunotherapy.
- The main focus today appears to be cancer immunotherapy.
- Tolerance is being sought for allergy and autoimmunity as well.
- The next several years will be critical for demonstrating commercial viability through high profile product launches in allergy and possibly cancer immunotherapy.
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