A Historical Perspective
Against All Odds

BIONEX

« AGAINST ALL ODDS »

Artemisinin Conference Madagascar
October 14th 2010
HOW IT ALL GOT STARTED BACK IN 2005
Brief Time Line of Bionexx Project
Time Line / Key Events of Bionexx Project (1/2)

- First mention of artemisinin late December 2004
- First Google of “artemisinin” and “artemisia annua” on January 4th 2005
- Mid February 2005, attendance at Institut Pasteur of meeting on artemisinin and ACTs
- First launch of cultivation in Lac Aloatra region with our partner Juslain Raharinaivo in March 2005 with an ambitious objective of 100 hectares
- First International conference on artemisinin in June 2005 in Arusha
- Formal startup of the BIONEXX Company in July 2005
- From the onset, Bionexx ambitioned to be a key player in artemisinin supply.
- BIONEXX focused at the time on 2 issues:
  - Trying to master cultivation of artemisia annua in malagasy type conditions (biomass yield and artemisinin content)
  - Trying to select and effective and competitive technology for extraction and purification of artemisia annua with the perspective of setting up in due course a “greenfield” operation
Time Line / Key Events of Bionexx Project
(2/2)

- Late 2005 initial contacts taken with INDENA investigating the possibility of collaborating on the artemisinin project knowing that this company already had extraction capacity and activity here in Madagascar.

- February 2006 signature of an agreement that would ultimately lead to the purchase on Indena Madagascar and that would also include de development by Indena Italy of the extraction/purification protocols for artemisinin.

- In the mean time Bionexx focused almost exclusively on the biomass side ramping up production and optimizing efficiency parameters.

- Late 2007, finalization of extraction/purification protocols by Indena and startup of industrial scale primary extraction in the Fianaranstoa based plant.

- February 2008, finalization of acquisition of Indena Madagascar which also included the setup of a supply agreement between INNOVEXX (ex Indena Madagascar) and INDENA in Italy for the pre existing activities (prunus africana, green tea, vanilla, centella asiatica..)

- From February 2008 to date we have focused our efforts on 2 fronts
  - Improving our competitiveness at the Fianarantsoa extraction plant (energy,...)
  - **Focusing on the three pillars of artemisinin competitiveness**
Critical Parameters Affecting Competitiveness in Artemisinin ($/kg)

The Three Pillars

- Artemisinin Content Of Artemisia Annua Leaf (%)
- Cost per kg Of Artemisinin (in $/kg)
- Cost Of Artemisia Annua Leaf (U.S. $ per Metric Ton)
- Efficiencies of Selected Extraction and Purification Technologies (%) Extraction/purification costs
Range of values of Critical Parameters Determining Artemisinin Cost per kg

<table>
<thead>
<tr>
<th></th>
<th>LOW</th>
<th>HIGH</th>
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<tbody>
<tr>
<td>1</td>
<td>Artemisinin leaf Content (%)</td>
<td>0.60%</td>
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<tr>
<td>2</td>
<td>Cost of leaf ($/MT)</td>
<td>900</td>
</tr>
<tr>
<td>3</td>
<td>Efficiency (from leaf to cristal %)</td>
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</tr>
<tr>
<td></td>
<td>Cost of Extraction/Purification ($/MT)</td>
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<thead>
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</thead>
<tbody>
<tr>
<td></td>
<td>Art. Content</td>
<td>AA leaf Cost ($/MT)</td>
<td>Ind. Eff. (%)</td>
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<tr>
<td>1</td>
<td>0.60%</td>
<td>900</td>
<td>60%</td>
</tr>
<tr>
<td>2</td>
<td>0.60%</td>
<td>1100</td>
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<td>15</td>
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<tr>
<td>16</td>
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</table>
There is a wide spread between the most competitive and the least competitive scenarios of the critical competitiveness factors. This clearly calls for optimization of these parameters.
Critical Parameters Affecting Competitiveness in Artemisinin ($/kg)

- Artemisinin Content Of Artemisia Annua Leaf (%)
- Cost per kg Of Artemisinin (in $/kg)
- Cost Of Artemisia Annua Leaf (U.S. $ per Metric Ton)
- Efficiencies of Selected Extraction and Purification Technologies (%) Extraction/Purification Costs
Critical Parameters Affecting Competitiveness in Artemisinin ($/kg)

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- Efficiencies of Selected Extraction and Purification Technologies (%)
  Extraction/Purification Costs
Critical Parameters Affecting
The cost of artemisinin ($/kg)

- The fully loaded cost of Artemisia Annua dry matter:
  - Purchasing cost from outgrower
  - Logistic costs
  - Field management costs
  - R&D costs
  - Depreciation
  - Overhead

- Since there is a significant amount of fixed costs, even in outgrower mode there is an impact of biomass per hectare on the fully loaded leaf costs

- The artemisinin content of the leaf at extractor entry stage which includes all the post harvest and storage costs.

- Choice of extraction purification technology. The major parameters are:
  - Overall efficiency (from leaf to pure cristal form)
  - Variable costs (solvents, energy...)
  - Investment related depreciation costs
Critical Parameters Affecting Competitiveness in Artemisinin ($/kg)

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Artemisinin Content in Artemisia Annua Leaf

• Bionexx benefited early on in the project from a local strain (initially imported from Vietnam). At the time there was no hybrid seeds available. This allowed for an effective commercial startup.

• What are the determining factors?
  
  – Intrinsic performance of the strain
  – Maturity at harvest
  – Agricultural conditions (soil quality, nutrients, fertilizers..)
  – Sampling protocol (part of plant, 100 plants..)
  – Drying protocols, transport, storage of AA leaf
  – **Analytical protocol**

• Without a fully vetted, accurate and reproductible protocol it is very hard to optimize industrial efficiencies.
Typical Artemisia Annua Content Dynamics

Artemisinin (%) Seasonal variation (2006) - Fifamanor Farm (Black Soil)
Critical Parameters Affecting Competitiveness in Artemisinin ($/kg)

- Cost of Artemisia Annua Leaf (U.S. $ per Metric Ton)
- Artemisinin Content of Artemisia Annua Leaf (%)
- Cost per kg of Artemisinin (in $/kg)
- Efficiencies of Selected Extraction and Purification Technologies (%)

Diagram showing the relationships between these parameters.
## Initial Bionexx project Objectives

<table>
<thead>
<tr>
<th>Cultivated Areas</th>
<th>Hectares</th>
<th>AA Dry Matter (MT)</th>
<th>MT Dry Matter</th>
<th>Yield MT/ha</th>
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<td>Industrial</td>
<td>Outgrower</td>
<td>Industrial</td>
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<td></td>
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<td>400</td>
<td>50</td>
<td>800</td>
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<td>400</td>
<td>100</td>
<td>800</td>
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<tr>
<td>2007 Dry Season Campaign</td>
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<td>200</td>
<td>450</td>
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<td><strong>2008 Rainy Season Campaign</strong></td>
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<tr>
<td><strong>2009 Rainy Season Campaign</strong></td>
<td>900</td>
<td>500</td>
<td>400</td>
<td>1 000</td>
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<tr>
<td>2009 Dry Season Campaign</td>
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<tr>
<td><strong>2010 Rainy Season Campaign</strong></td>
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<tr>
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<tr>
<td>2011 Dry Season Campaign</td>
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<tr>
<td><strong>2012 Rainy Season Campaign</strong></td>
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<td>400</td>
<td>1 000</td>
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<tr>
<td>2012 Dry Season Campaign</td>
<td>700</td>
<td>400</td>
<td>300</td>
<td>600</td>
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</table>

| Total                                  | 9 800    | 5 950              | 3 850        | 10 505      | 7 700        | 18 205       | 1,9          |
Projections of Artemisia Annua fully loaded Costs
($ per MT)

Coûts d’achat Artemisia Annua ($ par TM)
Logistique ($ par TM)
Encadrement Paysannat ($ par TM)
Recherche et Developpement ($ par TM)
Amortissements ($ par TM)
Coûts Siège ($ par TM)

Coûts Totaux ($ par TM)
Tonnage MP Feuille AA (en TM)

<table>
<thead>
<tr>
<th>Year</th>
<th>Coûts d’achat</th>
<th>Logistique</th>
<th>Encadrement Paysannat</th>
<th>Recherche et Developpement</th>
<th>Amortissements</th>
<th>Coûts Siège</th>
<th>Coûts Totaux</th>
<th>Tonnage MP Feuille AA</th>
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<td>$1,893</td>
<td>$69</td>
<td>$367</td>
<td>$200</td>
<td>$417</td>
<td>$418</td>
<td>$1,893</td>
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<td>$69</td>
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<td>$69</td>
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<tr>
<td>2012</td>
<td>$921</td>
<td>$69</td>
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<td>$480</td>
<td>$480</td>
<td>$480</td>
<td>$921</td>
<td>2,000</td>
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<tr>
<td>2013</td>
<td>$921</td>
<td>$69</td>
<td>$480</td>
<td>$480</td>
<td>$480</td>
<td>$480</td>
<td>$921</td>
<td>2,000</td>
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<tr>
<td>2014</td>
<td>$921</td>
<td>$69</td>
<td>$480</td>
<td>$480</td>
<td>$480</td>
<td>$480</td>
<td>$921</td>
<td>2,000</td>
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<tr>
<td>2015</td>
<td>$908</td>
<td>$69</td>
<td>$480</td>
<td>$480</td>
<td>$480</td>
<td>$480</td>
<td>$908</td>
<td>2,000</td>
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Achieved Results and Mid Term Objectives (Hectares)

- Total Hectares
- Outgrower Program
- Captive Production
Achieved Results and Mid Term Objectives
(Artemisia Annua Dry Matter tonnage)
## Bionexx Field Management Head Count

<table>
<thead>
<tr>
<th></th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
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<tr>
<td>Outgrower Relays</td>
<td>0</td>
<td>0</td>
<td>71</td>
<td>90</td>
<td>162</td>
<td>170</td>
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<td>Technicians</td>
<td>2</td>
<td>4</td>
<td>7</td>
<td>7</td>
<td>20</td>
<td>23</td>
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<td>Area Managers</td>
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<td>2</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>4</td>
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<tr>
<td>General Management</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
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<tr>
<td><strong>Total Bionexx Head Count</strong></td>
<td><strong>3</strong></td>
<td><strong>7</strong></td>
<td><strong>82</strong></td>
<td><strong>100</strong></td>
<td><strong>189</strong></td>
<td><strong>200</strong></td>
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CAPTIVE PRODUCTION
FAHARETANA FARM
CAPTIVE ARTEMISIA ANNUA: FAHARETANA FARM (ANTANANARIVO)
Critical Parameters Affecting Competitiveness in Artemisinin ($/kg)

- Artemisinin Content Of Artemisia Annua Leaf (%)
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- Cost Of Artemisia Annua Leaf (U.S. $ per Metric Ton)
- Efficiencies of Selected Extraction and Purification Technologies (%) Extraction/Purification Costs
Bionexx’s Competitiveness Objectives

Fully loaded costs
En $ par Kg
Bionexx Artemisinin Offer to the market
Bionexx Artemisinin Offer to Market
2010-2015

Metric Tons

Theoretical Artemisinin Tonnage (MT)
Available to market (MT)
BIONEXX/INNOVEXX: The last Five Years

- BIONEXX/INNOVEXX has achieved a certain number of milestones:
  - Bionexx has put in place a new cultivation in Madagascar with an emphasis on quality and tracability. The system in place will allow over the next three years to reach our objective of 2000 MT of leaf production per year.
  - Bionexx is on track to achieve its 2015 1,5% objective.
  - BIONEXX’s unique position as sole operator in artemisinin in Madagascar allows for a long term and competitive situation.
  - The selection of technologies for extraction and purification has taken a lot of time but will result in an extremely efficient and competitive process.
  - In summary we have a competitive raw material (cost and artemisinin content), efficient technologies and a very motivated management team.
3 different organisation for production:

- **Industrial Cultivation** (BIONEXX do the cultivation in its own rented farms)
- **Small farmers** (Bionexx provides coaching, pre-financing of inputs, but delegates the production to the peasants)
- **Providers** (BIONEXX make a light monitoring of the campaign but delegates the production to private companies or associations …)
The five month growing time offer the possibility of 3 campaigns per Year in Madagascar.

We have a flowering of the plant in march
Experimentation
Training
ORGANIZATION OF A REGION

REGION MANAGER (4)

OFFICE
Buyer (4)
Secretary (4)

Technical Supervisor (28)

Foot soldier (125)
Nursery keeper (200)

SMALL FARMERS
**SMALL FARMER MANAGEMENT**

- **Outgrower**
  - 1 contract / farmer / campaign
  - + 6 visits of technical supervisor during growing period

- **Village**
  - 1 synthesis sheet / campaign
  - + 1 visit / week of technical supervisor

- **Sector**
  - 1 synthesis sheet / campaign

**Reliable information for each campaign**
A regulatory structure important for:

- Ensure the technical success of farmers
- Material traceable and ensure quality
- Popularize and densify our business

The artemisia plant is new to farmers, its cultivation requires close supervision. The optimisation of the content of artemisinin alone justifies the establishment of this structure.
We have developed a software for the production

**It offers:**

• The management of the campaigns
• A geo localisation of the production
• The follow-up of the production
• The analysis of the results
• The cost management
• The management of logistic (Inputs, Leaves...)
• The traceability of the production
Ex: Fianarantsoa Region
### Fianarantsoa Region development

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<tr>
<th></th>
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<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
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<td><strong>Surface cultivée (ha)</strong></td>
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<td>8</td>
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<td>19</td>
<td>60</td>
<td>60</td>
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