About Biotage

Headquartered in Uppsala, Sweden

• Three Centers of Excellence
  – **Uppsala, Sweden**
    Research & Development
  – **Charlottesville VA, U.S.A.**
    Instrument Manufacturing
  – **Cardiff, Wales**
    Cartridge Manufacturing and resin development
Coming Together

- 2003 Pyrosequencing acquires Personal Chemistry and Biotage
- Parent adopts Biotage AB name
- 2 Divisions
  - Discovery Chemistry Group (DCG)
    - Personal Chemistry AB + Biotage Inc.
      Microwave Synthesis + Flash Purification
  - Biosystems Group
    - Pyrosequencing
• Mission
  – To be the preferred supplier of a complete suite of innovative high quality tools that work together to improve experimental success rates and productivity in discovery chemistry
• Synthetic Route - Pathfinder MW reaction database
• Synthesis - Initiator Microwave Synthesizers
• Purification - Biotage Flash Systems & Cartridges
Working Together
Biotage Acquires Argonaut Technologies’ Business

- Synthetic Route - Pathfinder MW reaction database
- Synthesis - Initiator Microwave Synthesizer
- Work-up - Solid-bound Reagents & Scavengers and SPE
- Purification - Biotage Flash Systems & Cartridges
- Sample Preparation - IST Sorbents
- Process Development - Advantage Series & Endeavor
Biotage Acquires Evaporation Technology from Vapourtec

- Synthetic Route - Pathfinder MW reaction database
- Synthesis - Initiator Microwave Synthesizer
- Work-up - Solid-bound Reagents & Scavengers and SPE
- Purification - Biotage Flash Systems & Cartridges
- Evaporation - V10 vortex and vacuum evaporation system
- Sample Preparation - IST Sorbents
- Process Development - Advantage Series & Endeavor
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Discovery Chemistry
- Serves three prominent market segments, Medicinal Chemistry, Analytical Chemistry and Process Development
- Primary products, which are utilized by research organizations worldwide, include;
  - microwave synthesis, resins and solid phase extraction (SPE), flash purification cartridges and systems, and reaction screening instruments.

Biosystems
- Serves two primary market segments Clinical and Pharmaceutical
- Products include; PyroMark for methylation, SNP and mutation analysis and Pyro Gold reagents.
• Largest range of innovative and integrated discovery chemistry tools for synthesis, work-up, purification, evaporation and sample preparation.

• Solutions for research and development through clinical trials and manufacturing

• Product synergies work together to improve drug discovery and remove process bottlenecks.
40% identify Synthesis as the dominant bottleneck.

50% of Pharma Discovery Directors identify Purification as the dominant bottleneck to Drug Discovery.

Automating Synthesis, Workup and Purification is seen as a major technique to speed up Drug Discovery.

The use of solid-bound scavengers and reagents in Microwave Synthesis is a growing trend among all Pharmaceutical chemists.

HTC labs are also incorporating solid-phase extraction (SPE) techniques into work-up and purification.
Discovery Chemistry Tool-kit

**Synthesis**
- Extremely fast reactions
- High yield and purity
- Enables “impossible” reactions
- Reproducible

**Work-up**
- Vortex and Vacuum rapid evaporation
  - Organic solvents & water
  - Flexible formats
  - Flow or batch mode
  - Effective re-dissolution

**Purification**
- Automated flash purification
  - 1-10 cartridges in unattended operation
  - TLC to gradient method development

**Evaporation**
- Solid-bound Reagent and Scavenger
  - Simplifies purification
  - Facilitates reaction chemistry
Biotage Pathfinder Web is the world’s largest online database of established methods for microwave synthesis.

**PathFinder Data**

**Coverage:** 2000 – present

**Focus:** Microwave synthesis with explicit experimental details

**Source:** ~70% Biotage internal unpublished results; ~15% contributions from scientific partners; ~15% published data

**Size:** > 3,800 reactions

**Updates:** Monthly, online
Microwave heating allows for rapid ramping to ideal conditions and quick quenching of the reaction... reacting purer compounds with higher yields in a fraction of the time.

**Initiator EXP**
Available with automated 8 and 60 position robots

**4 Vial Sizes — Volume range is unique to Biotage**

- 10 – 20 mL
- 2 – 5 mL
- 0.5 – 2 mL
- 0.2 – 0.5 mL
Using resins with MW chemistry

- The latest tools and techniques incorporate the use of solid-bound reagents, catalysts and scavengers in microwave synthesis.

- Key transformations
  - Amidation
  - Aryl-aryl bond formation (Suzuki reaction)
  - Reductive amination
  - Oxidation
  - Acid-catalyzed reactions
  - Base-catalyzed reaction
  - Electrophiles scavenging
Work-up

Polymer-bound scavengers and reagents simplify product workup by substituting filtration for traditional techniques, such as liquid-liquid extraction and chromatography.

- Biotage scavengers and reagents
  - 13 varieties of polymer-bound scavengers
  - 18 varieties of polymer-bound reagents
  - 6 new silica-bound reagents
Scavengers

- Resin-bound scavengers bind to excess reagents and by-products, for removal by simple filtration.
- The desired product remains in solution.
- Functionalities that are resin-bound do not react with each allowing multiple scavengers may be used simultaneously in a single step.
• Polymer-bound reagents are functional polymers that perform synthetic transformations in the same way as their solution counterparts.
• Excess reagent and by-products remain attached to the resin, while the end product is purified by simple filtration.
Biotage has created a Resin tool-kit that contains solid-bound scavengers and reagents for the following applications:

**Amidation Reaction:**
- PS-Carbodiimide
- PS-HOBt (HL)
- RGT-ACTU
- MP-TsOH(65)
- MP-Carbonate

**Reductive Amination**
- MP-Triacetoxyborohydride
- MP-Cyanoborohydride
- MP-TsOH(65)
- PS-Isocyanate
- MP-Isocyanate
- PS-Benzaldehyde

**Coupling:**
- PS-Triphenylphosphine
- PS-PPh3-Pd 1g
- MP-Carbonate
- MP-TsOH(65)
- PS-DEAM

**Oxidation:**
- MP-TsO-TEMPO
Sample work-up products

- Scavengers
  - Excess reagent removal
  - Silica-based
  - Resin-based

- Catch & Release products
  - Capture then release compound of interest

- Filtration tools
  - Particulate removal

- Water removal cartridges
  - Organic sample dehydration

- Phase separation tools
  - In-lieu of separatory funnels
Prepacked flash purification cartridges and automated flash purification systems reduce compound separation time and increase throughput.

**SP1 EXP**
Automated single column flash purification system upgrades to the SP4 sequential 4-column system

**Flash Cartridges**
Sizes range from 4.5 g - 40,000 g of silica. FLASH+ and Samplet cartridge insert improve sample loading and purification efficiency
A novel approach
- New vaporizing technology delivers rapid low temperature evaporation of solvents from vials under precisely controlled conditions with no bumping
• The V-10 is rewriting the rules of solvent evaporation in drug discovery

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Time to evaporate 10ml of pure solvent at 40 ºC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>V-10</td>
</tr>
<tr>
<td>DMF</td>
<td>4 minutes</td>
</tr>
<tr>
<td>Water</td>
<td>8 minutes</td>
</tr>
<tr>
<td>Methanol</td>
<td>4 minutes</td>
</tr>
<tr>
<td>Cyclo-hexane</td>
<td>1 minute</td>
</tr>
</tbody>
</table>
Typical Applications

- Evaporation of solvents in a general bench chemistry environment
- Open access drying of prep. HPLC fractions
- Open access drying of fractions following FLASH chromatography
- Concentration of extractions and / or dilute HPLC fractions for analysis
- Solvent exchange following synthesis by flow chemistry
- Continuous drying of compounds following synthesis or purification by flow chemistry
Sample Preparation for Analysis

Sorbent chemistries are used for sample preparation with Bioanalytical, Clinical, Environmental, Food and Forensic applications.

- **Pharmaceutical**
  - Bioanalytical (ADME Tox)
  - Purification SPE

- **Forensic**
  - Doping Control
  - DOA

- **Environmental**

- **Agrochemical / Food**
Bioanalysis in drug discovery

• Quantitative determination of drug candidate concentrations
  – biological fluids (in vivo testing)
  – cells and tissues (in vitro testing)

• Drug development stages
  – Discovery Support
  – Pre-clinical
  – Clinical

• Analysis by LC-MS/MS
Biotage IST Sorbents and formats

International Sorbent Technologies
Founded in 1992, internationally recognized as a high-quality sorbent manufacturer. Acquired from Argonaut June 2005

Well-plate format
Either fixed or array

Bulk format

Column format
Process Synthesis Instrumentation

**Atlantis**
Atlantis Pressure Reactor System – (one) 100 ml reactor and (one) 1 L pressure reactor workstation.

**Advantage Series 2410**
Bench-top reaction screening workstation.

**Advantage Series 3400**
Multi-reactor Process Chemistry workstation.

**Advantage Series 4100**
Process scale-up reactor

**Endeavor**
Catalyst Screening System
Process-scale MW Synthesis

- Advancer — Batch microwave synthesizer for the scale-up of organic synthesis.
Biotage offers the largest range of innovative and integrated discovery chemistry tools for synthesis, work-up, purification, evaporation and analysis. With solutions for research and development through clinical trials and manufacturing, Biotage focuses on removing process bottlenecks using automation, while improving success rates with reproducible results. This scope of expertise is unique to Biotage and allows us to offer unprecedented customer service and technical support.
ONE Company, ONE Point of Contact, Many Solutions...

Working Together