



From Customer-centric User Research to Data Visualization App:

A Journey of Developing Modules to Support Exploratory Biomarker Analysis

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Disclaimer

The views expressed in this talk are those of the speakers and not necessarily those of Boehringer Ingelheim

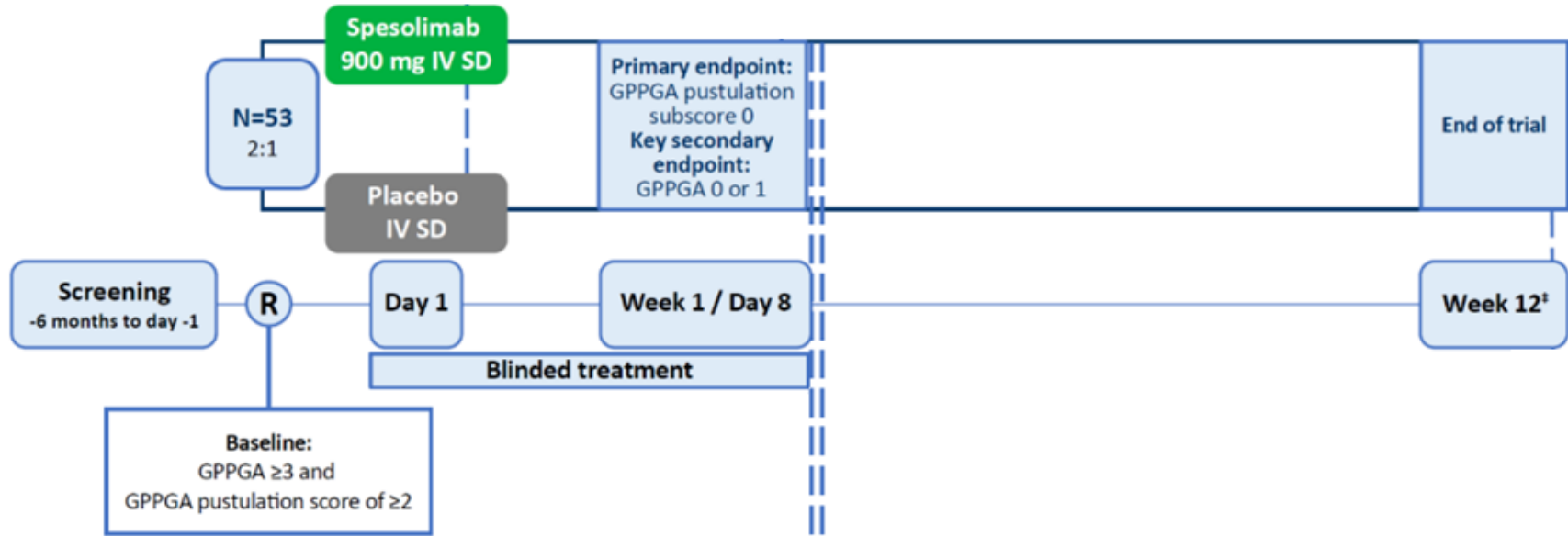
Background: Generalized Pustular Psoriasis (GPP)

- Rare, potentially life-threatening skin disease
- Characterized by episodes of widespread eruption of sterile visible pustules
- Can occur with or without systemic inflammation
- Flares are characteristic of the clinical course

Background: Spesolimab

- In GPP the IL-36 pathway plays a key role
- Inhibition of IL-36 signaling may provide effective targeted treatment
- Spesolimab is a IL-36 receptor inhibitor to treat GPP

Effisayil™ 1 - Spesolimab in Generalized Pustular psoriasis



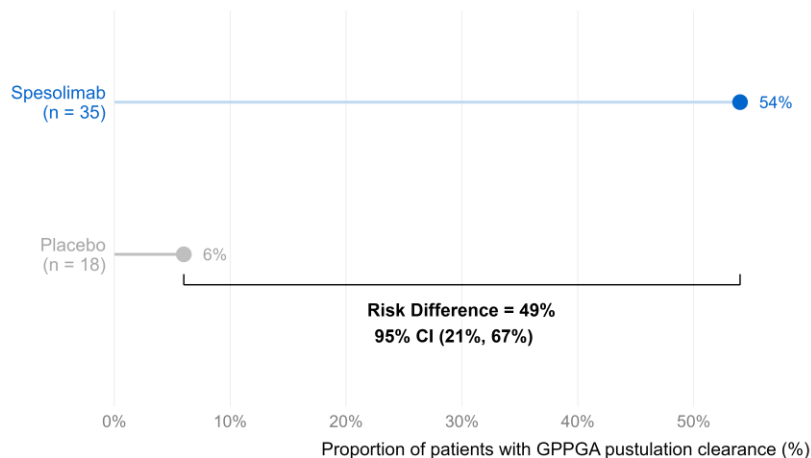
Evidence of effectiveness

+

Strong mechanistic support

- Binary efficacy endpoint

Spesolimab rapidly controlled symptoms of GPP flare skin within 1 week of treatment



- Continuous efficacy endpoint

Role of Biomarkers

- Provide strong mechanistic support
- Provide further insights into GPP disease and mode of action of spesolimab
- Biomarker focused presentations and publications

Protein Biomarker Analysis and Visualization

Objectives

- Multiple protein biomarkers (from various pathways) should be analyzed and visualized
- Link to main clinical efficacy endpoint(s) should be presented
- Integration of relevant baseline variables and/or other binary efficacy endpoints of interest

Protein Biomarker Analysis and Visualization

Objectives

- Multiple protein biomarkers (from various pathways) should be analyzed and visualized → heatmap
- Link to main clinical efficacy endpoint(s) should be presented → sorting of patients via waterfall plot
- Integration of relevant baseline variables and/or other binary efficacy endpoints of interest → extra panels

Protein Biomarker Analysis and Visualization

Variety of options for the implementation

- Which biomarkers to be integrated and how to order?
- What clinical, baseline and/or subgroup features should be integrated?
- Which time point(s) are most important?
- What scaling and coloring is most suitable?
- Should certain patients be excluded (e.g. due to unavailability of data)?
- What kind of labels are required?



Use interactive App to assess the options



WHY? - Motivation

From:

Static Data Review
Focus: Tables

2.3.2 Clinical laboratory evaluation

2.3.2.1 LABPCS - Possibly clinically significant abnormalities

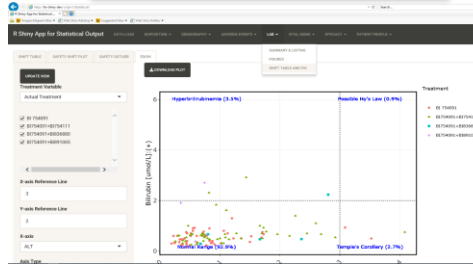
Parameter Treatment	N	Number analyzed ¹	Low		High	
			N	%	N	%
Lab parameter 1						
Treat 1	xxx	xxx	xxx	xx.x	xxx	xx.x
<Treat k>	xxx	xxx	xxx	xx.x	xxx	xx.x
Lab parameter n>						
Treat 1	xxx	xxx	xxx	xx.x	xxx	xx.x
<Treat k>	xxx	xxx	xxx	xx.x	xxx	xx.x

¹ Subjects with no possibly clinically significant abnormality at baseline. Empty column or lines indicate that there are no corresponding rules defined. Subjects may be counted twice per parameter and treatment when meeting low and high



To:

Interactive data review
Focus: Graphics



And beyond...

Storytelling with data

- ▶▶▶ Existing gap for **interactive, real-time data visualization** to support
 - trial oversight & decision making
 - statistical novelties

- Web-based
- Linked outputs
- Real-time and interactive

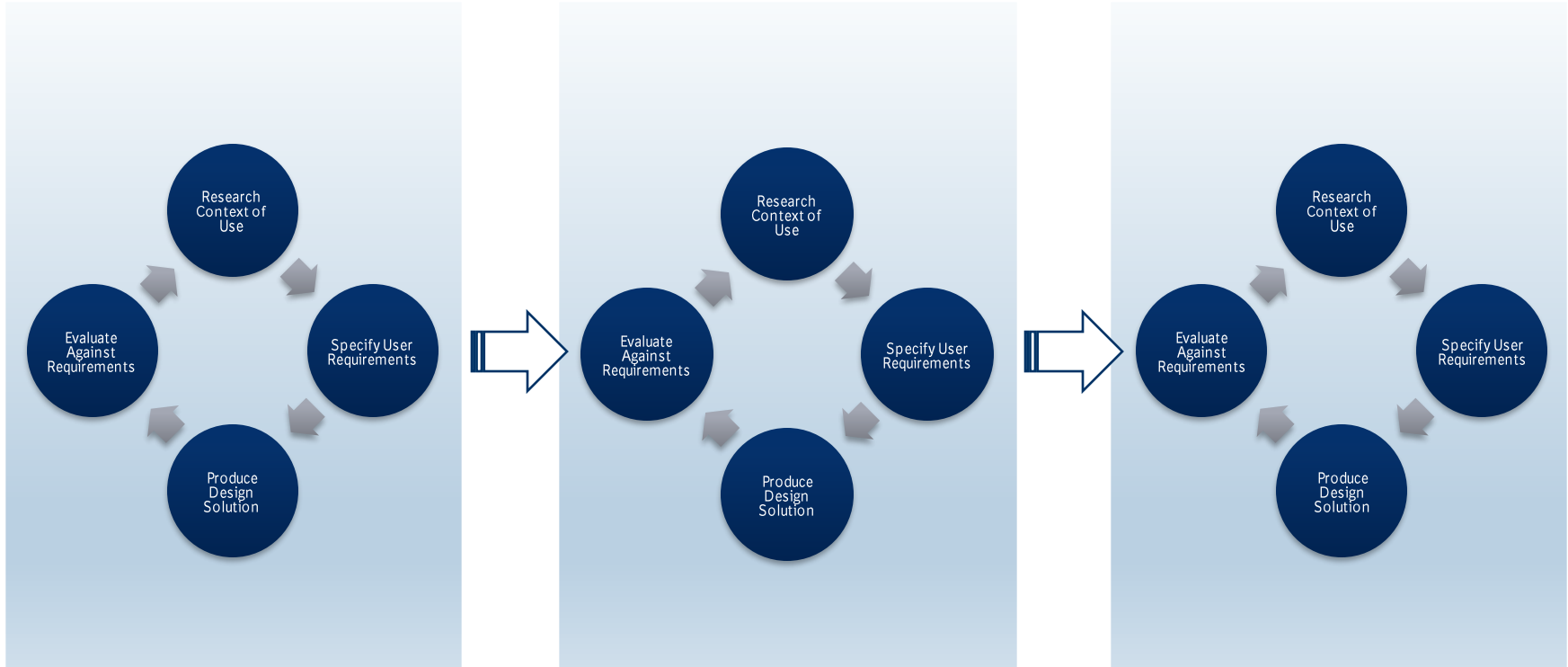
- ▶▶▶ **Effective & focused** trial oversight
 - Review, incl. deep-dive option
 - Align & share insights during meetings
- ▶▶▶ **Faster clinical insights generation and more agile decision making**

- ▶▶▶ **Unleash the power of data through visualization:** Consider new ways of reviewing and presenting data
- ▶▶▶ Use advanced graphics to support implementation of new statistical methods
- ▶▶▶ Guide your team through the data

From Customer-centric User Research to Data Visualization App



From Customer-centric User Research to Data Visualization App

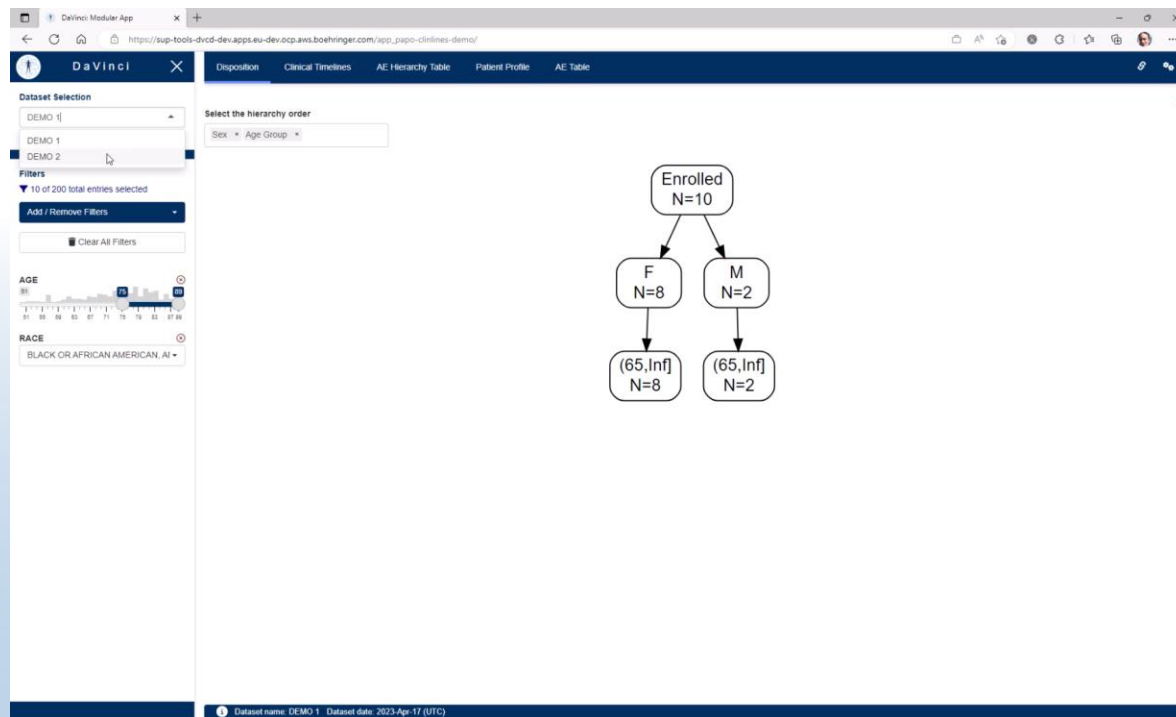


The Concept of the Modular Approach

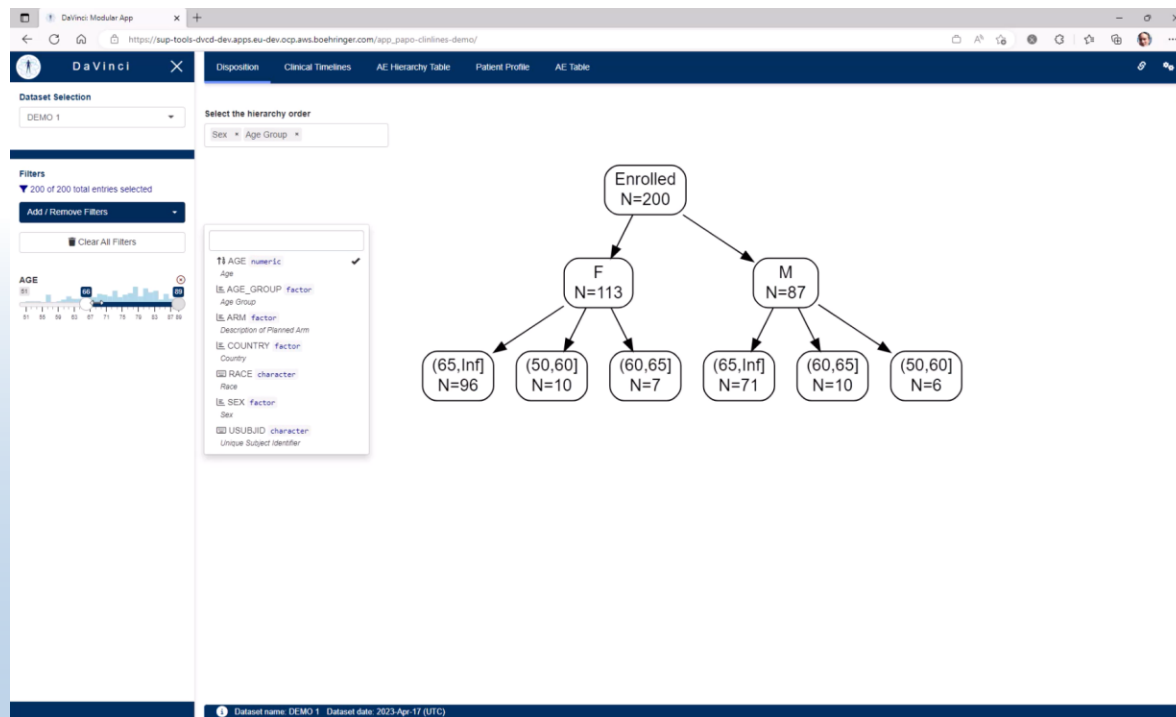
- DaVinci Modules are functional building blocks composable into customized Apps
- This customization enables the building of Apps according to **trial** and **project-specific** needs
- Enables teams to use best-practice templates with a common look-and-feel
- The Hosting Platform allows to create, integrate and deploy Apps.



Modular Approach: Data Selection



Modular Approach: Subject filtering by Continuous Variable



Modular Approach: Subject filtering by Categorical Variable

The screenshot displays the Da Vinci Modular App interface. On the left, the 'Dataset Selection' dropdown is set to 'DEMO 1'. Below it, the 'Filters' section shows '113 of 200 total entries selected'. The 'AGE' filter is set to '(65, Inf]'. The 'RACE' filter is set to 'BLACK OR AFRICAN AMERICAN, AI'. A table of filtered subjects is visible, with columns for 'Select All' and 'Deselect All'. The table lists the following categories and counts:

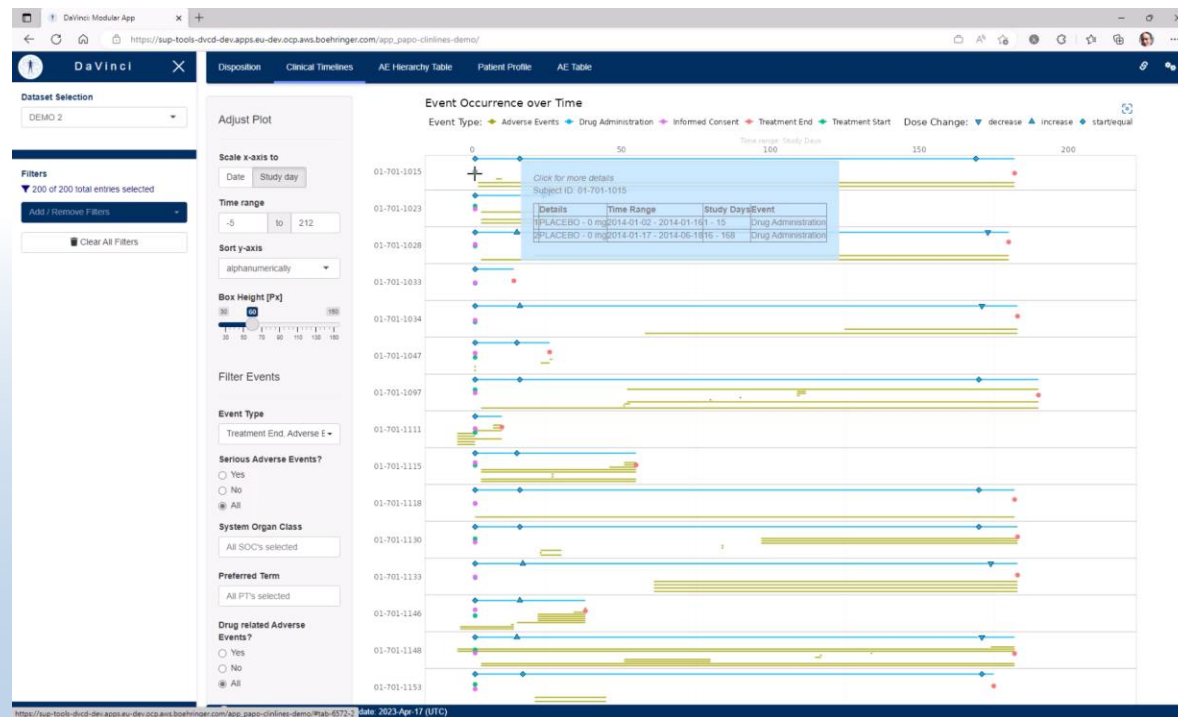
Category	Count
WHITE	103 / 178
BLACK OR AFRICAN AMERICAN	10 / 21
AMERICAN INDIAN OR ALASKA NATIVE	0 / 1

On the right, a flowchart illustrates the filtering process:

```
graph TD; A[Enrolled N=113] --> B[F N=68]; A --> C[M N=45]; B --> D["(65, Inf] N=68"]; C --> E["(65, Inf] N=45"];
```

The bottom status bar indicates: Dataset name: DEMO 1, Dataset date: 2023-Apr-17 (UTC).

Modular Approach: The Clinical Timelines Module



Modular Approach: The Patient Profile Module

The screenshot displays the 'Patient Profile' module in the Da Vinci application. The interface includes a navigation bar with tabs for Disposition, Clinical Timelines, AE Hierarchy Table, Patient Profile, and AE Table. The Patient Profile tab is active, showing patient information and a data table of adverse events.

Patient Information

Select Patient ID: 01-701-1015

Study Site Identifier: 701
Race: WHITE
RFICDT: 2014-01-02
Date of Discontinuation/Completion: 2014-07-02

Age: 63
Ethnicity: HISPANIC OR LATINO
Date of First Exposure to Treatment: 2014-01-02
Reason for Discontinuation: Completed

Sex: F
Description of Planned Arm: Placebo
Date of Last Exposure to Treatment: 2014-07-02
Actual Treatment for Period 01: Placebo

Data Table

Select Domain: Adverse Events, Concomitant Medication, Lab, Vital signs

Select Extra Columns: USUBJID, ASTDT, AENDT, AEDECOD, AE

Unique Subject Identifier	Analysis Start Date	Analysis End Date	Dictionary-Derived Term	Primary System Organ Class	Severity/Intensity	Serious Event	Causality	Action Taken with Study Treatment	Outcome of Adverse Event
1	01-701-1015	2014-01-03	APPLICATION SITE ERYTHEMA	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	MILD	N	PROBABLE		NOT RECOVERED/NOT RESOLVED
2	01-701-1015	2014-01-03	APPLICATION SITE PRURITUS	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	MILD	N	PROBABLE		NOT RECOVERED/NOT RESOLVED
3	01-701-1015	2014-01-09	2014-01-11	DIARRHOEA	GASTROINTESTINAL DISORDERS	MILD	N	REMOTE	RECOVERED/RESOLVED

Showing 1 to 3 of 3 entries

Graphical Display

Please Select Parameter for Lab plot: Please Select Parameter for Vital Sign plot:

Dataset name: DEMO 2 Dataset date: 2023-Apr-17 (UTC)

Modular Approach: The Patient Profile Module

The screenshot displays the 'Patient Profile' module in the Da Vinci application. The interface includes a navigation bar with tabs for Disposition, Clinical Timelines, AE Hierarchy Table, Patient Profile (active), and AE Table. On the left, there is a 'Dataset Selection' dropdown set to 'DEMO 2' and a 'Filters' section showing '200 of 200 total entries selected' with a 'Clear All Filters' button.

Patient Information

Select Patient ID: 01-701-1015

Study Site Identifier: 701
Race: WHITE
RFICDT: 2014-01-02
Date of Discontinuation/Completion: 2014-07-02

Age: 63
Ethnicity: HISPANIC OR LATINO
Date of First Exposure to Treatment: 2014-01-02
Reason for Discontinuation: Completed

Sex: F
Description of Planned Arm: Placebo
Date of Last Exposure to Treatment: 2014-07-02
Actual Treatment for Period 01: Placebo

Data Table

Select Domain: Adverse Events (selected), Concomitant Medication, Lab, Vital signs

Select Extra Columns: USUBJID, ASTDT, AENDT, AEDECOD, AE

Reset Columns Order

Unique Subject Identifier	Analysis Start Date	Analysis End Date	Dictionary-Derived Term	Primary System Organ Class	Severity/Intensity	Serious Event	Causality	Action Taken with Study Treatment	Outcome of Adverse Event
1	01-701-1015	2014-01-03	APPLICATION SITE ERYTHEMA	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	MILD	N	PROBABLE		NOT RECOVERED/NOT RESOLVED
2	01-701-1015	2014-01-03	APPLICATION SITE PRURITUS	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	MILD	N	PROBABLE		NOT RECOVERED/NOT RESOLVED
3	01-701-1015	2014-01-09	2014-01-11	DIARRHOEA	GASTROINTESTINAL DISORDERS	MILD	N	REMOTE	RECOVERED/RESOLVED

Showing 1 to 3 of 3 entries

Graphical Display

Please Select Parameter for Lab plot: Please Select Parameter for Vital Sign plot:

Dataset name: DEMO 2 Dataset date: 2023-Apr-17 (UTC)

Modular Approach: Bookmark functionality

The screenshot shows a web application interface for 'Da Vinci' with a 'Bookmarked application link' dialog box. The dialog box contains the following text:

Bookmarked application link

https://sup-loc-0vcd-dev.apps.eu-dev.ocp.aws.boehringer.com/app_papo-cliniles-demo?state_id=6582fa70a210a

The current state of this application has been stored on the server. Press Ctrl-C to copy.

Dismiss

The background interface includes a 'Dataset Selection' dropdown set to 'DEMO 2', 'Patient Information' section with fields for Patient ID (01-701-1015), Study Site Identifier (701), Race (WHITE), RPIDT (2014-01-02), and Date of Discontinuation/Completion (2014-07-02). The 'Data Table' section shows a table with columns for Unique Subject Identifier, Analysis Start Date, Analysis End Date, Dictionary-Derived Term, Primary System Organ Class, Severity/intensity, Serious Event, Causality, Action Taken with Study Treatment, and Outcome of Adverse Event. The table contains three rows of data.

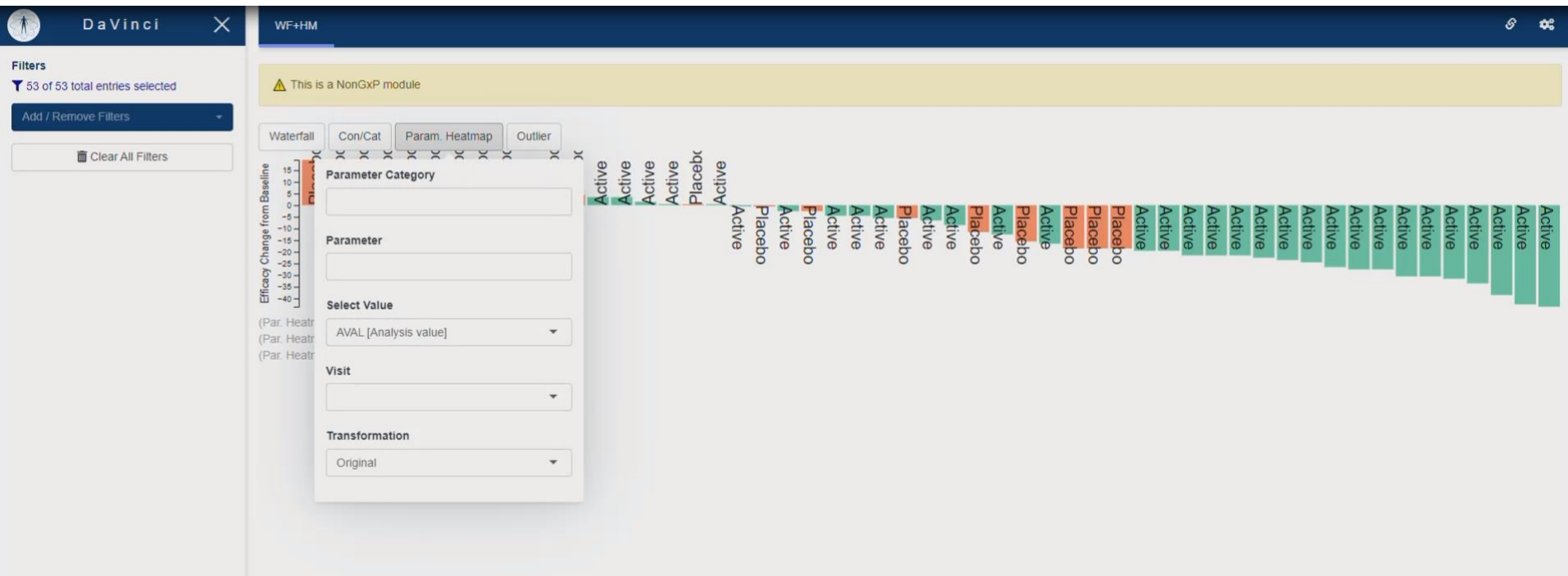
Unique Subject Identifier	Analysis Start Date	Analysis End Date	Dictionary-Derived Term	Primary System Organ Class	Severity/intensity	Serious Event	Causality	Action Taken with Study Treatment	Outcome of Adverse Event
1	01-701-1015	2014-01-03	APPLICATION SITE ERYTHEMA	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	MILD	N	PROBABLE		NOT RECOVERED/NOT RESOLVED
2	01-701-1015	2014-01-03	APPLICATION SITE PRURITUS	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	MILD	N	PROBABLE		NOT RECOVERED/NOT RESOLVED
3	01-701-1015	2014-01-09	2014-01-11	DIARRHOEA	GASTROINTESTINAL DISORDERS	MILD	N	REMOTE	RECOVERED/RESOLVED

Backup (App demo)

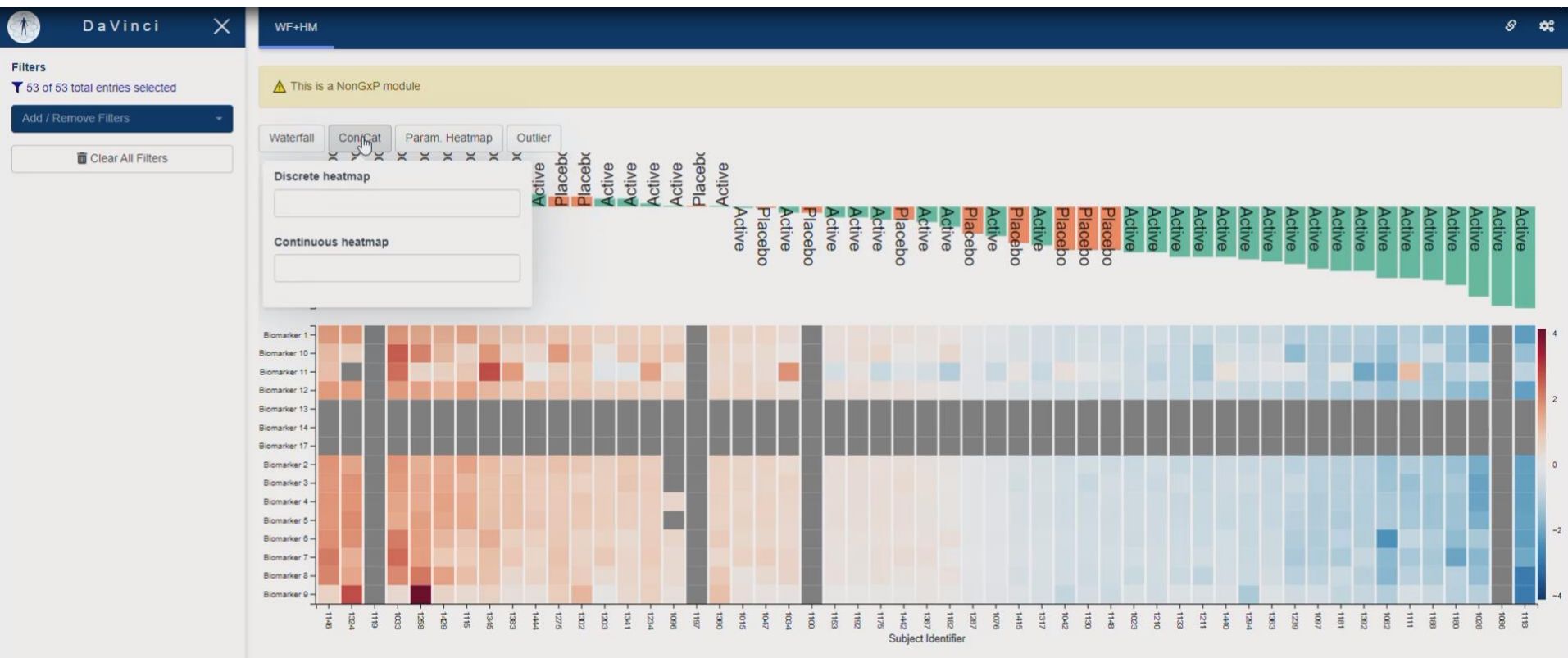
Note: Artificial dummy data has been used for the demonstration

The screenshot displays the Da Vinci software interface. At the top, the header shows 'Da Vinci' and 'WF+HM'. A yellow warning banner states 'This is a NonGxP module'. Below this, there are navigation tabs: 'Waterfall', 'Con/Cat', 'Param. Heatmap', and 'Outlier'. The 'Waterfall' tab is active, showing a visualization of data points for 'TRTPN [Planned Treatment (N)]'. The data is grouped by 'STUDYID [Study Identifier]', with 20 columns labeled 'CDISCPILLOT01'. A settings panel on the left includes a 'Use parameter' checkbox, a 'Value' dropdown set to 'TRTPN [Planned Treatment (N)]', a 'Grouping' dropdown set to 'STUDYID [Study Identifier]', and 'TRTPN' range options for 'Min' and 'Max'. The visualization shows a series of vertical bars, all of which are green, representing the dummy data.

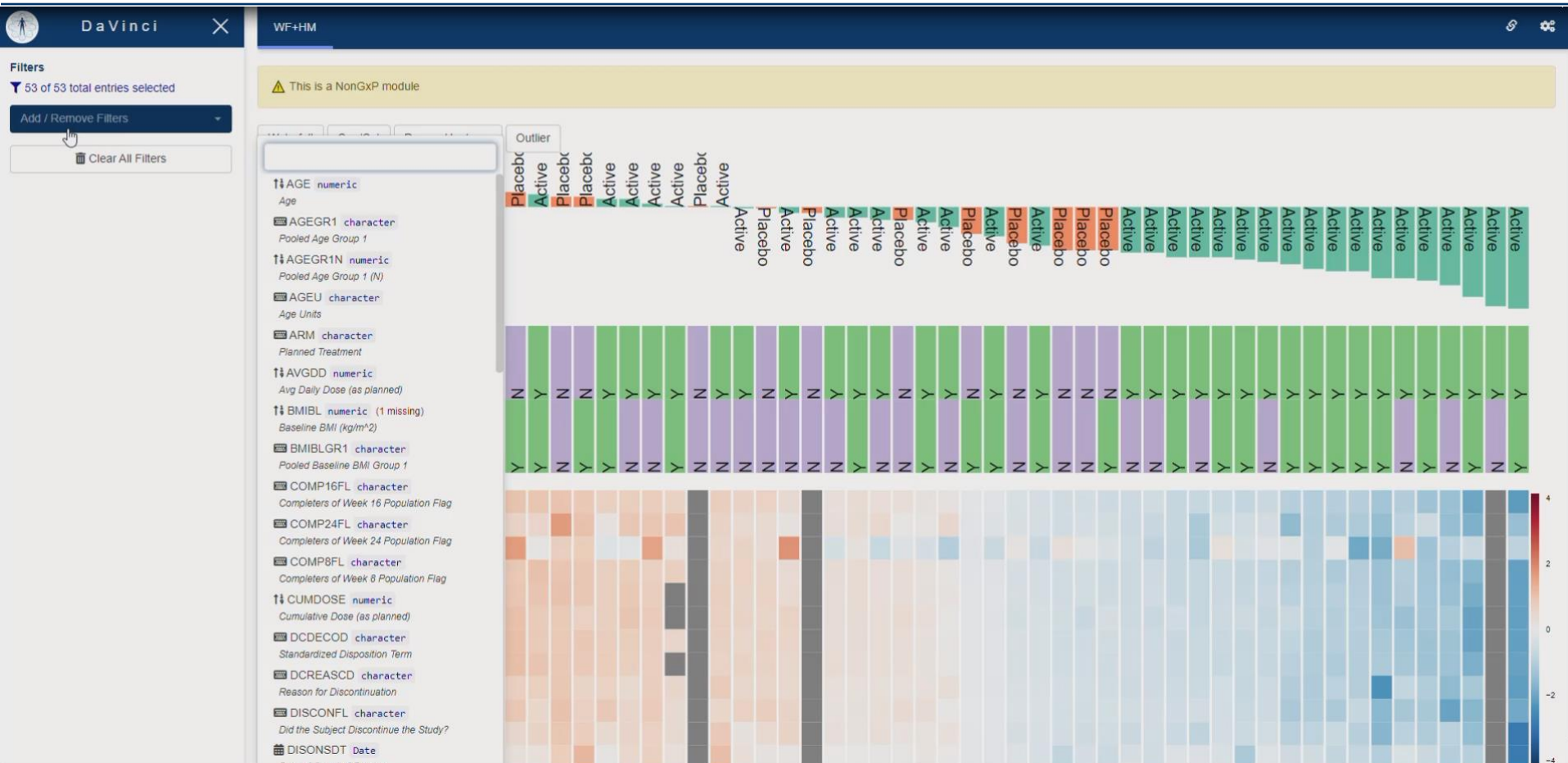
Note: Artificial dummy data has been used for the demonstration



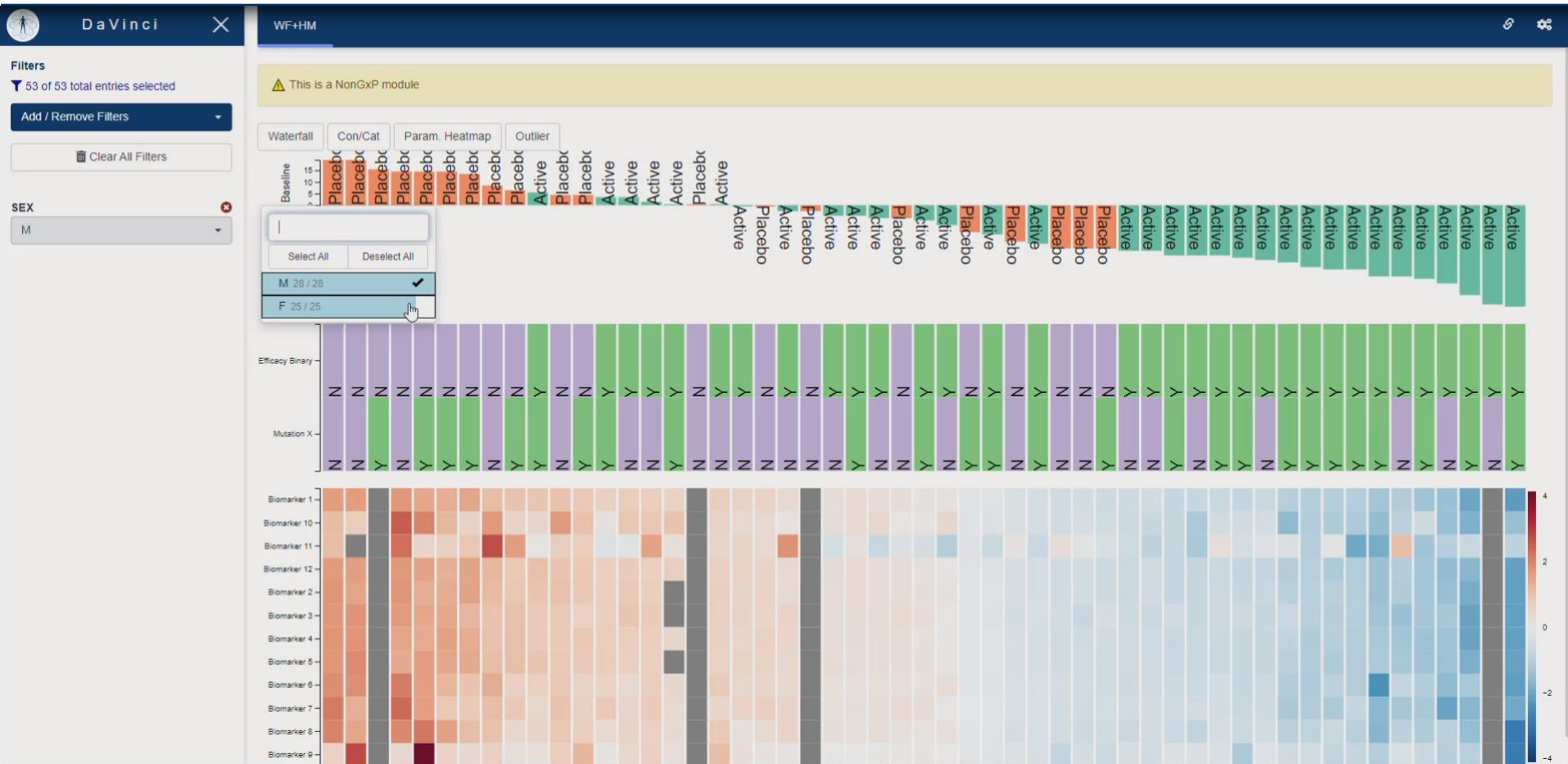
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