

High-Mannose *N*-Glycans

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Cell-surface oligosaccharides appended to proteins and lipids are key binding epitopes in many critical biological processes, including bacterial infection, cell development and the immune response. Understanding these processes at the molecular level requires access to a wide range of oligosaccharides of known structure to support investigations of enzyme substrate binding and specificity, to screen for carbohydrate binding proteins, and to develop assays for enzymic activity. Omicron Biochemicals, Inc. was awarded Small Business Innovation Research (SBIR) grants by the National Institutes of Health (NIH) in 2013 and 2015 to increase the commercial availability of these oligosaccharides, thus facilitating progress in this field.

Omicron has focused on the synthesis of oligosaccharides derived from the parent high-mannose oligosaccharide (14-mer) that is transferred *en-bloc* to polypeptides during translation. During Phase I of our project, we pursued a “bottom-up” synthetic approach instead of a “top-down” approach to overcome the limitations of the latter. All five *O*-glycosidic linkages found in naturally occurring high-mannose *N*-glycans of human glycoproteins were constructed, leading to the preparation of thirty-two (32) oligosaccharides (3- to 6-mers) using a generalized chemical approach. During Phase I of this project, Omicron chemists developed robust synthetic protocols and gained knowledge, experience and technical know-how to extend the chemical space in a subsequent Phase II project.

As of May 2017, Omicron has made over 100 high-mannose *N*-glycans available for purchase on their website at www.omicronbio.com. Products range from simple mannobiose compounds to mannose nonasaccharides. Mannose oligosaccharides with one or two *N*-acetyl-glucosamine residues are available, as are mannose oligosaccharides with a mannose phosphate residue

As Omicron continues to expand the variety of obtainable high-mannose *N*-glycans, methods will be developed to array this extensive library to support anticipated screening efforts by investigators in the glycoscience community.

In the following list of products, we omit the configurational symbol, the letter denoting ring size, and the locant of the anomeric carbons. All of the monosaccharide units are pyranose rings of the D-form with the anomeric carbon at C1.

Omicron Catalog

Number Product Name

DIS-010 Man α -2Man

DIS-011 Man α -3Man

DIS-012 Man α -6Man

TRI-007 Man α -2Man α -2Man
TRI-008 Man α -2Man α -3Man
TRI-009 Man α -2Man α -6Man
TRI-010 Man α -3Man α -6Man
TRI-005 Man α -6Man α -6Man
TRI-006 Man α -3[Man α -6]Man
TRI-011 Man α -4[Man α -6]Man
TET-016 Man α -2Man α -2Man α -2Man
TET-004 Man α -2Man α -2Man α -3Man
TET-006 Man α -2Man α -2Man α -6Man
TET-005 Man α -2Man α -3Man α -6Man
TET-007 Man α -2Man α -6Man α -6Man
TET-010 Man α -2Man α -3[Man α -6]Man
TET-009 Man α -2Man α -6[Man α -3]Man
TET-011 Man α -3Man α -6[Man α -3]Man
TET-019 Man α -6Man α -6[Man α -3]Man
TET-008 Man α -3[Man α -6]Man α -6Man
TET-015 Man α -3[Man α -4][Man α -6]Man
PEN-007 Man α -2Man α -2Man α -3[Man α -6]Man
PEN-003 Man α -2Man α -3Man α -6[Man α -3]Man
PEN-015 Man α -2Man α -6Man α -6[Man α -3]Man
PEN-008 Man α -2Man α -3[Man α -6]Man α -6Man
PEN-002 Man α -2Man α -6[Man α -3]Man α -6Man
PEN-005 Man α -2Man α -3[Man α -2Man α -6]Man
PEN-006 Man α -2Man α -3[Man α -3Man α -6]Man
PEN-004 Man α -2Man α -3[Man α -6Man α -6]Man
PEN-012 Man α -6Man α -4[Man α -6Man α -6]Man
PEN-001 Man α -3[Man α -6]Man α -6[Man α -3]Man
HEX-003 Man α -2Man α -2Man α -3[Man α -3Man α -6]Man
HEX-004 Man α -2Man α -2Man α -3[Man α -6Man α -6]Man
HEX-011 Man α -2Man α -3Man α -6[Man α -2Man α -3]Man
HEX-010 Man α -2Man α -6Man α -6[Man α -2Man α -3]Man
HEX-001 Man α -2Man α -3[Man α -2Man α -6]Man α -6Man
HEX-012 Man α -2Man α -3[Man α -6]Man α -6[Man α -3]Man

HEX-014 Man α -2Man α -6[Man α -3]Man α -6[Man α -3]Man
HEX-002 Man α -3[Man α -6]Man α -6[Man α -2Man α -3]Man
OLI-005 Man α -2Man α -2Man α -3[Man α -2Man α -3Man α -6]Man
OLI-006 Man α -2Man α -2Man α -3[Man α -2Man α -6Man α -6]Man
OLI-010 Man α -2Man α -2Man α -3[Man α -3[Man α -6]Man α -6]Man
OLI-012 Man α -2Man α -3[Man α -2Man α -6]Man α -6[Man α -3]Man
OLI-007 Man α -2Man α -3[Man α -6]Man α -6[Man α -2Man α -3]Man
OLI-013 Man α -2Man α -6[Man α -3]Man α -6[Man α -2Man α -3]Man
OLI-014 Man α -2Man α -3[Man α -2Man α -6]Man α -6[Man α -2Man α -3]Man
OLI-008 Man α -2Man α -3[Man α -6]Man α -6[Man α -2Man α -2Man α -3]Man
OLI-015 Man α -2Man α -6[Man α -3]Man α -6[Man α -2Man α -2Man α -3]Man
OLI-009 Man α -2Man α -3[Man α -2Man α -6]Man α -6[Man α -2Man α -2Man α -3]Man

Mannose oligosaccharides with one α -Glc residue

TRI-030 Glc α -3Man α -2Man
TET-047 Glc α -3Man α -2Man α -2Man
PEN-027 Glc α -3Man α -2Man α -3[Man α -6]Man
PEN-026 Glc α -3Man α -3[Man α -3Man α -6]Man
PEN-025 Glc α -3Man α -3[Man α -6Man α -6]Man
HEX-029 Glc α -3Man α -2Man α -2Man α -3[Man α -6]Man
OLI-029 Glc α -3Man α -2Man α -2Man α -3[Man α -3Man α -6]Man
OLI-030 Glc α -3Man α -2Man α -2Man α -3[Man α -6Man α -6]Man
OLI-028 Glc α -3Man α -2Man α -3[Man α -3[Man α -6]Man α -6]Man

Mannose oligosaccharides with one D-GlcNAc residue

TRI-015 Man α -3Man β -4GlcNAc
TRI-016 Man α -6Man β -4GlcNAc
TET-020 Man α -2Man α -3Man β -4GlcNAc
TET-021 Man α -3Man α -6Man β -4GlcNAc
TET-022 Man α -6Man α -6Man β -4GlcNAc
TET-018 Man α -3[Man α -6]Man β -4GlcNAc
PEN-017 Man α -2Man α -2Man α -3Man β -4GlcNAc
PEN-018 Man α -2Man α -3Man α -6Man β -4GlcNAc
PEN-019 Man α -2Man α -6Man α -6Man β -4GlcNAc

PEN-013 Man α -3Man α -6[Man α -3]Man β -4GlcNAc
PEN-014 Man α -6Man α -6[Man α -3]Man β -4GlcNAc
HEX-019 Man α -2Man α -2Man α -3[Man α -6]Man β -4GlcNAc
HEX-008 Man α -2Man α -3Man α -6[Man α -3]Man β -4GlcNAc
HEX-009 Man α -2Man α -6Man α -6[Man α -3]Man β -4GlcNAc
HEX-018 Man α -2Man α -3[Man α -3Man α -6]Man β -4GlcNAc
HEX-017 Man α -2Man α -3[Man α -6Man α -6]Man β -4GlcNAc
HEX-016 Man α -2Man α -3[Man α -6]Man α -6Man β -4GlcNAc
HEX-020 Man α -2Man α -6[Man α -3]Man α -6Man β -4GlcNAc
HEX-015 Man α -3[Man α -6]Man α -6[Man α -3]Man β -4GlcNAc
OLI-019 Man α -2Man α -2Man α -3[Man α -3Man α -6]Man β -4GlcNAc
OLI-020 Man α -2Man α -2Man α -3[Man α -6Man α -6]Man β -4GlcNAc
OLI-021 Man α -2Man α -3[Man α -2Man α -6]Man α -6Man β -4GlcNAc
OLI-026 Man α -2Man α -2Man α -3[Man α -3[Man α -6]Man α -6]Man β -4GlcNAc

Mannose oligosaccharides with two D-GlcNAc residues

TRI-019 Man β -4GlcNAc β -4GlcNAc
TET-032 Man α 1-3Man β -4GlcNAc β -4GlcNAc
TET-031 Man α 1-6Man β -4GlcNAc β -4GlcNAc
PEN-023 Man α -2Man α -3Man β -4GlcNAc β -4GlcNAc
PEN-016 Man α -3[Man α -6]Man β -4GlcNAc β -4GlcNAc
HEX-013 Man α -2Man α -2Man α -3Man β -4GlcNAc β -4GlcNAc
HEX-023 Man α -2Man α -3Man α -6Man β -4GlcNAc β -4GlcNAc
HEX-024 Man α -2Man α -6Man α -6Man β -4GlcNAc β -4GlcNAc
HEX-026 Man α -2Man α -3[Man α -6]Man β -4GlcNAc β -4GlcNAc
HEX-028 Man α -3Man α -6[Man α -3]Man β -4GlcNAc β -4GlcNAc
HEX-027 Man α -6Man α -6[Man α -3]Man β -4GlcNAc β -4GlcNAc
HEX-025 Man α -3[Man α -6]Man α -6Man β -4GlcNAc β -4GlcNAc
OLI-023 Man α -2Man α -3[Man α -3Man α -6]Man β -4GlcNAc β -4GlcNAc
OLI-024 Man α -2Man α -3[Man α -6Man α -6]Man β -4GlcNAc β -4GlcNAc
OLI-011 Man α -2Man α -2Man α -3[Man α -3Man α -6]Man β -4GlcNAc β -4GlcNAc
OLI-018 Man α -2Man α -2Man α -3[Man α -6Man α -6]Man β -4GlcNAc β -4GlcNAc
OLI-025 Man α -2Man α -3[Man α -2Man α -6]Man α -6Man β -4GlcNAc β -4GlcNAc
OLI-016 Man α -2Man α -2Man α -3[Man α -2Man α -3Man α -6]Man β -4GlcNAc β -4GlcNAc

OLI-017 $\text{Man}\alpha\text{-2Man}\alpha\text{-2Man}\alpha\text{-3}[\text{Man}\alpha\text{-2Man}\alpha\text{-6Man}\alpha\text{-6}]\text{Man}\beta\text{-4GlcNAc}\beta\text{-4GlcNAc}$

Mannose oligosaccharides with one mannose phosphate residue (Man4P or Man6P)

DIS-020 $\text{Man4P}\alpha\text{-6Man}$ disodium salt

DIS-017 $\text{Man6P}\alpha\text{-2Man}$ disodium salt

DIS-018 $\text{Man6P}\alpha\text{-3Man}$ disodium salt

DIS-019 $\text{Man6P}\alpha\text{-6Man}$ disodium salt

TET-044 $\text{Man}\alpha\text{-2Man}\alpha\text{-3}[\text{Man4P}\alpha\text{-6}]\text{Man}$ disodium salt

TET-043 $\text{Man}\alpha\text{-2Man}\alpha\text{-3}[\text{Man6P}\alpha\text{-6}]\text{Man}$ disodium salt

TET-041 $\text{Man}\alpha\text{-6Man}\alpha\text{-6}[\text{Man6P}\alpha\text{-3}]\text{Man}$ disodium salt

TET-042 $\text{Man6P}\alpha\text{-6Man}\alpha\text{-6}[\text{Man}\alpha\text{-3}]\text{Man}$ disodium salt

PEN-022 $\text{Man}\alpha\text{-2Man}\alpha\text{-2Man}\alpha\text{-3}[\text{Man6P}\alpha\text{-6}]\text{Man}$ disodium salt

PEN-021 $\text{Man}\alpha\text{-2Man}\alpha\text{-3Man}\alpha\text{-6}[\text{Man6P}\alpha\text{-3}]\text{Man}$ disodium salt

PEN-020 $\text{Man}\alpha\text{-2Man}\alpha\text{-3}[\text{Man6P}\alpha\text{-6Man}\alpha\text{-6}]\text{Man}$ disodium salt