Supporting Information Appendix

Structural basis for sulfation-dependent self-glycan recognition by the human immune-inhibitory receptor Siglec-8

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SI Appendix:

Chemical synthesis of 6-sulfo sialyl Lewis^x (**2**), 6′-sulfo sialyl Lewis^x (**3**) and 6,6′-disulfo sialyl Lewis^x (**4**)

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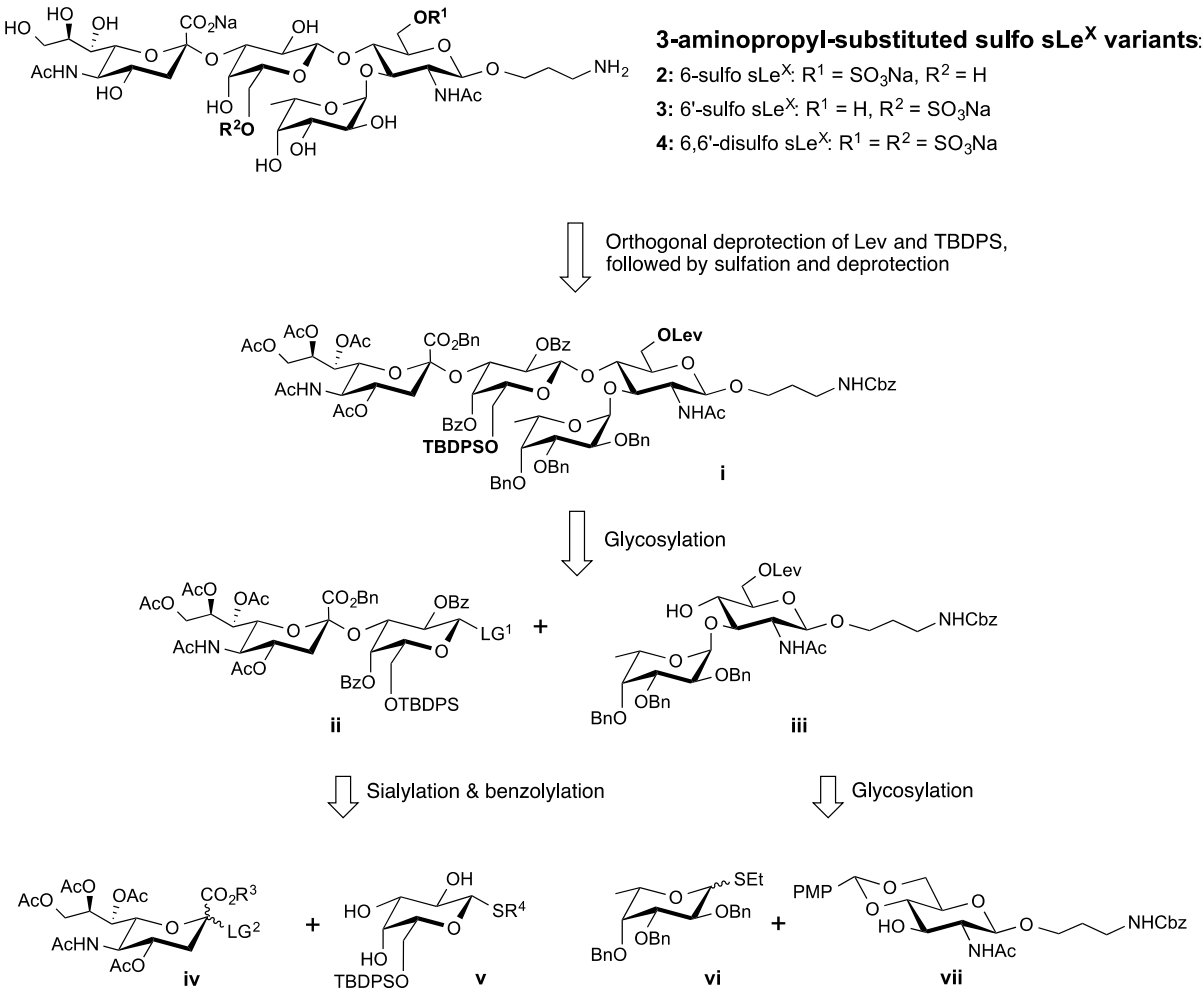
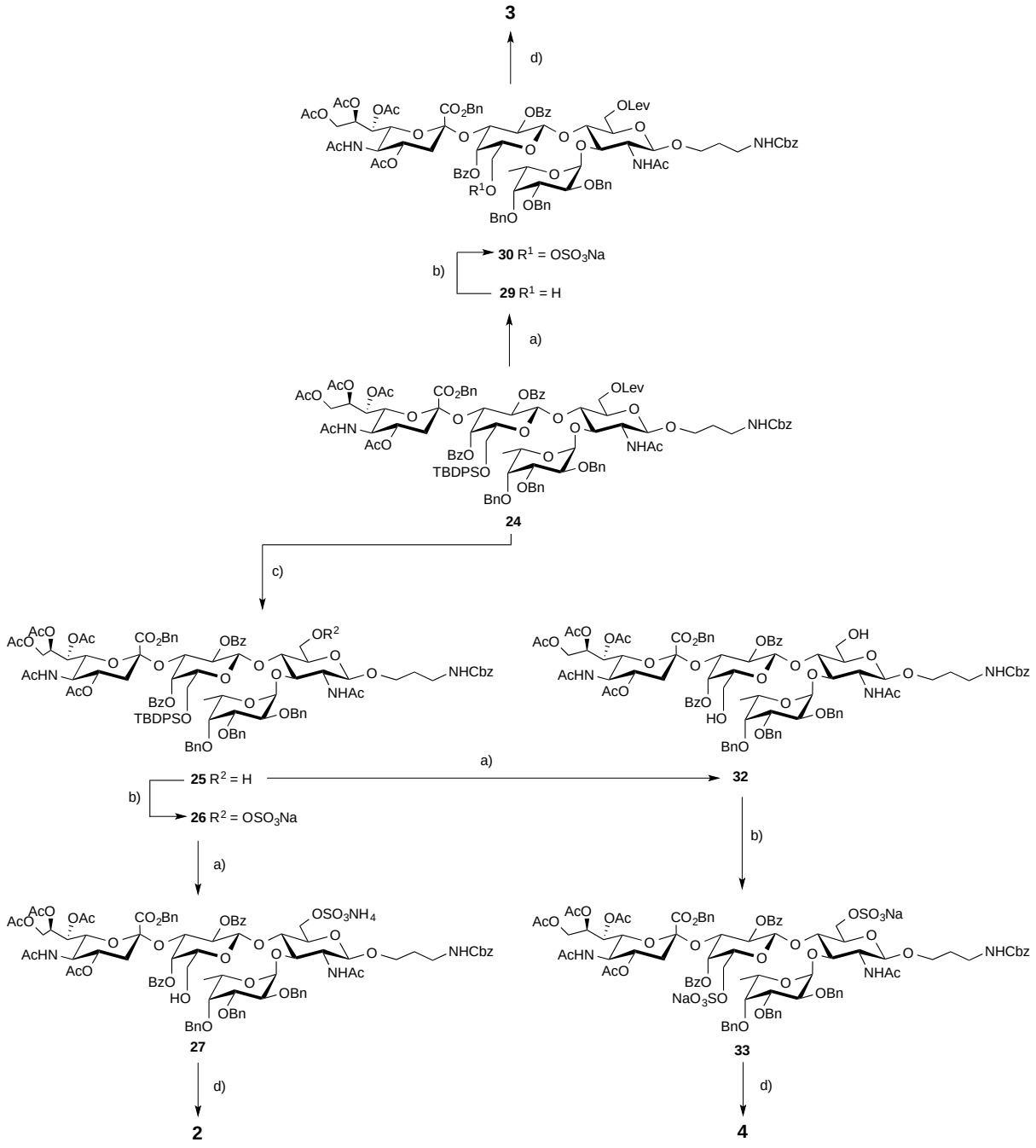


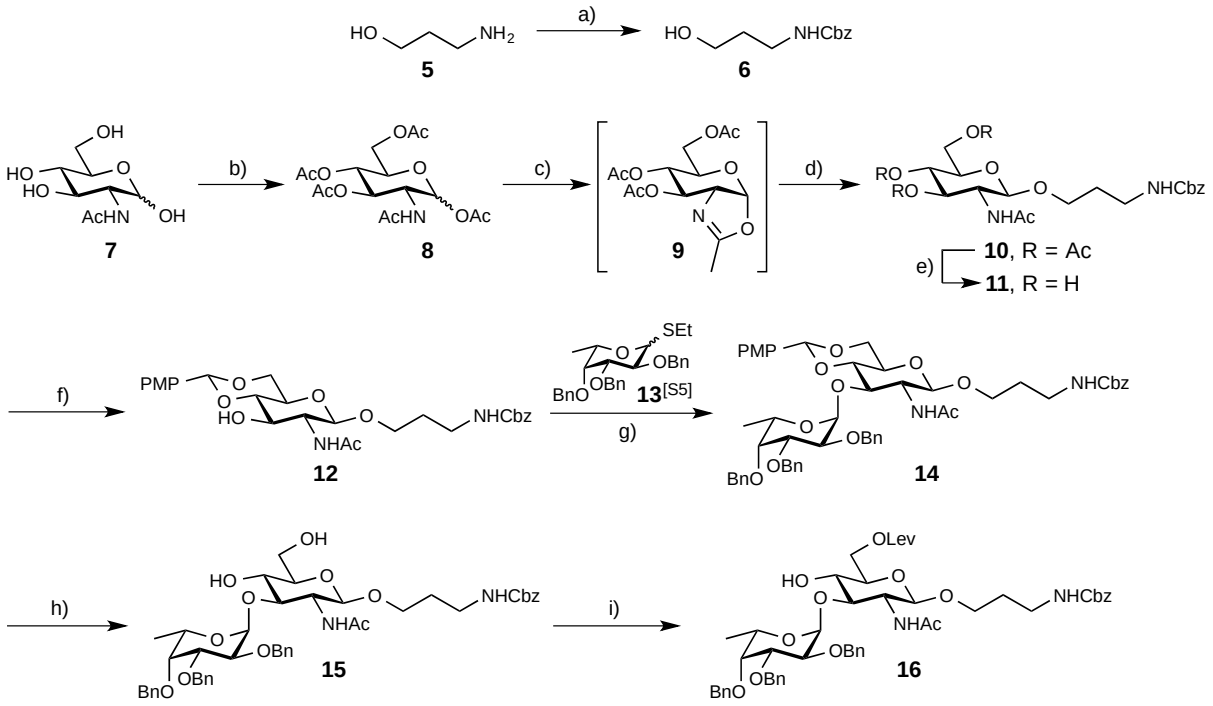
Scheme S1. Retrosynthesis of sulfated sialyl Lewis^x variants



Scheme S2. Reagents and conditions. a) HF-pyr, pyr, 2 h, 86% for **27**, 91% for **29**, 88% for **32**; b) Pyr-SO_3, DMF, 4 h, 67% for **26**, 85% for **30**; 90% for **33**; c) H_2NNH_2-AcOH, 83%; d) NaOMe, MeOH; then H_2, $Pd(OH)_2$, 54%; for **2**, 44% for **3** and 63% for **4**.

General Methods. NMR spectra were recorded on a Bruker Avance DMX-500 (500 MHz) spectrometer. Assignment of ^{1}H and ^{13}C NMR spectra was achieved using 2D methods (COSY, HSQC, HMBC, TOCSY). Chemical shifts are expressed in ppm in relation to the residual solvent signals ($CHCl_3$, CHD_2OD and HDO) on the δ-scale. Coupling constants *J* are given in Hertz (Hz). Multiplicities were specified as follows: s (singlet), d (doublet), dd (doublet of a doublet), t (triplet), q (quartet), m (multiplet). Commercially available reagents were purchased from Fluka, Aldrich, Acros, and Abcr. Dichloromethane (DCM) and acetonitrile (MeCN) were dried by filtration over Al_2O_3 (Fluka, type 5016 A basic). *N*,*N*-dimethylformamide (DMF) was dried by distillation from calcium hydride. Methanol (MeOH) was dried by refluxing with sodium methoxide and distilled immediately before use. Molecular sieves were activated under vacuum at 500 ºC for 1 h immediately before use. Reactions were monitored by TLC using glass plates coated with silica gel 60 F_{254} (Merck) and visualized by using UV light and/or by charring with a molybdate solution (a 0.02 M solution of ammonium cerium sulfate dihydrate and ammonium molybdate tetrahydrate in 10% aq. H_2SO_4). Column chromatography was performed on a CombiFlash Companion (Teledyne-ISCO, Inc.) using RediSep normal phase disposable flash columns (silica gel, 40-63 μm). Reversed phase chromatography was performed on LiChroprepRP-18 (Merck, 40-63 μm). Electron spray ionization mass spectra (ESI-MS) were obtained on a Waters micromass ZQ. Optical rotations were measured using Perkin-Elmer polarimeter 341.

Synthesis of Fuc-Glc*N*Ac building block 16:



Scheme S3. a) CbzCl, $NaHCO_3$, H_2O, 0 °C to rt, overnight (88%); b) Ac_2O/pyridine, 24 h (78%); c) TMSOTf, DCM, 50 °C, overnight; d) **6**, TMSOTf, DCM, 50 °C, 8 h (45% over two steps); e) NaOMe/MeOH, 8 h (94%); f) *p*-anisol dimethyl acetal, *p*-TsOH·H_2O, DMF, overnight (72%); g) **7**, $CuBr_2$, *n*-Bu_4NBr, 2,6-di-*tert*-butylpyridine, MS 4 Å, DCM, DMF (93%); h) CAN, MeCN/H_2O, 0 °C to rt, 5 h (74%); i) levulinic acid, EDC, DMAP, DCM, -15 °C to 0 °C (66%).

Benzyl (3-hydroxypropyl)carbamate (6).(1, 2) To an ice-cooled mixture of $NaHCO_3$ (23.6 g, 281 mmol) and 3-aminopropan-1-ol (**5**, 25 mL, 327 mmol) in water (100 ml) benzyl chloroformate (23 mL, 161 mmol) was added dropwise. The solution was stirred at rt overnight and then DCM (100 ml) was added. The organic phase was washed with H_2SO_4/brine (pH ~ 1, 3 × 30 mL) and satd aq $NaHCO_3$ (30 mL), dried over Na_2SO_4, concentrated in vacuo, and washed with petroleum ether/ethyl ether to give **6** (29.4 g, 141 mmol, 88%) as an off-white solid.

2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucopyranoside (8).(3) To a solution of *N*-acetyl-D-glucosamine (**7**, 20.0 g, 90.5 mmol) in pyridine (80 mL) was added Ac_2O (100 mL) dropwise at 0 °C under argon. The reaction mixture was stirred at rt for 24 h and then evaporated to dryness. The residue was dissolved in DCM (100 mL), washed with brine (containing 0.05 M H_2SO_4) and satd aq $NaHCO_3$. The organic phase was dried with Na_2SO_4,

concentrated, and the crude product was recrystallized from EtOAc/heptane to yield **8** (27.4 g, 70.4 mmol, 78%, α/β 8:1) as a white solid.

3-([(Benzyloxy)carbonyl]amino)propyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (10). A solution of **8** (15.5 g, 39.8 mmol) and TMSOTf (8.30 mL, 46.0 mmol) in dry DCM (60 mL) was stirred overnight at 50 °C under argon. TLC monitoring (petroleum ether/acetone, 1.5:1) showed complete conversion to the oxazoline intermediate **9**.(4) Then, compound **6** (20.8 g, 99.6 mmol) was added in portions at rt and the mixture was stirred at 50 °C for 8 h. The reaction was quenched with satd aq $NaHCO_3$ (50 mL) and extracted with DCM (3 × 100 mL). The combined organic layers were dried over Na_2SO_4, concentrated, and the residue was purified by recrystallization from EtOAc/heptane to give **10** (5) (9.60 g, 17.8 mmol, 45%) as a white solid.

3-([(Benzyloxy)carbonyl]amino)propyl 2-acetamido-2-deoxy-β-D-glucopyranoside (11). A solution of **10** (8.44 g, 15.7 mmol) in MeOH (100 mL) was treated with 2.6 M NaOMe/MeOH (4 mL, 10.4 mmol) for 8 h at rt under argon. The mixture was neutralized with Dowex ion-exchange resin (H^+ form) to pH ~ 6 and concentrated to give **11** (5) (6.10 g, 14.8 mmol, 94%) as an off-white solid.

3-([(Benzyloxy)carbonyl]amino)propyl 2-acetamido-2-deoxy-4,6-*O*-(4-methoxy-benzylidene)-β-D-glucopyranoside (12). To a solution of **11** (6.10 g, 14.8 mmol) and *p*-toluenesulfonic acid monohydrate (600 mg, 3.16 mmol) in DMF (30 mL) was added *p*-anisol dimethyl acetal (10 mL) at rt under argon. After being stirred overnight, the reaction mixture was neutralized with NEt_3 (1 mL), and diluted with DCM (50 mL) and EtOAc (50 mL). After stirring for 30 min, the precipitate was filtered off and washed with EtOAc (30 mL) to give **12** (5.67 g, 10.7 mmol, 72%) as an off-white solid.

$[\alpha]_D^{20}$ -34.8 (*c* 0.40, DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 4.2 Hz, 1H), 7.39 (m, 7H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.67 (d, *J* = 1.7 Hz, 1H), 5.52 (s, 1H), 5.15 (d, *J* = 12.2 Hz, 1H), 5.08 (d, *J* = 12.2 Hz, 1H), 4.91 (dd, *J* = 9.4, 3.5 Hz, 1H), 4.27 (dd, *J* = 10.3, 5.0 Hz, 1H), 4.15 (d, *J* = 8.4 Hz, 1H), 3.96 (m, 1H), 3.74 (m, 7H), 3.57 (t, *J* = 9.2 Hz, 1H), 3.31 (m, 1H), 3.23 (m, 1H), 3.03 (dd, *J* = 14.3, 3.7 Hz, 1H), 2.05 (s, 3H), 1.84 (m, 1H), 1.52 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 174.17, 160.13, 157.34, 136.54, 129.77, 128.66, 128.45, 128.11, 127.71, 113.56, 101.85, 101.40, 81.84, 77.28, 77.02, 76.77, 74.18, 68.52, 67.20, 66.20, 65.82, 59.10, 55.30, 36.36, 30.34, 22.64; ESI-MS: *m/z*: Calcd for $C_{27}H_{34}N_2NaO_9$ $[M+Na]^+$: 553.2, found: 553.1.

3-([(Benzyloxy)carbonyl]amino)propyl (2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)-2-acetamido-2-deoxy-4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranoside (14). Fucose donor **13** (37) (810 mg, 1.70 mmol), acceptor **12** (616 mg, 1.13 mmol), 2,6-di-*tert*-butylpyridine (0.55 mL, 2.49 mmol), *n*-Bu_4NBr (546 mg, 1.70 mmol) and activated molecular sieves 4 Å (500 mg) were suspended in a mixture of DCM (5 mL) and DMF (2.5 mL) under argon. The mixture was stirred for 30 min at rt and then cooled to 0 °C. $CuBr_2$ (378mg, 1.70 mmol) was added, and the reaction mixture was stirred for 11 h at 0 °C and for another 24 h at rt. Then, the reaction mixture was quenched with NEt_3 (1 mL) and filtered through celite. The celite was washed with DCM, and the filtrate was concentrated. The residue was dissolved in DCM (100 mL, with 1 mL of NEt_3) and washed with brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, and evaporated in vacuum. The residue was purified by flash chromatography (petroleum ether/EtOAc) to afford **14** (1.01 g, 1.06 mmol, 93%) as an off-white solid.

$[\alpha]_D^{20}$ -94.1 (*c* 1.00, acetone); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (m, 22H), 6.85 (d, *J* = 8.7 Hz, 2H), 5.91 (d, *J* = 6.7 Hz, 1H), 5.44 (s, 1H), 5.21 (s, br, 1H), 5.10 (d, *J* = 12.4 Hz, 3H), 4.91 (d, *J* = 11.5 Hz, 1H), 4.85 (d, *J* = 11.3 Hz, 1H), 4.69 (m, 4H), 4.58 (d, *J* = 11.5 Hz, 1H), 4.29 (dd, *J* = 10.4, 4.8 Hz, 1H), 4.08 (m, 3H), 3.92 (dd, *J* = 10.2, 2.6 Hz, 1H), 3.88 (dd, *J* = 10.0, 4.9 Hz, 1H), 3.80 (s, 3H), 3.71 (t, *J* = 10.3 Hz, 1H), 3.57 (m, 2H), 3.35 (m, 4H), 1.70 (m, 5H), 0.88 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.76, 160.05, 156.56, 138.66, 138.58, 138.51, 136.81, 129.81, 128.58, 128.51, 128.41, 128.28, 128.18, 128.11, 128.06, 127.97, 127.56, 127.45, 127.32, 113.54, 101.48, 101.41, 98.28, 80.66, 79.80, 77.58, 75.48, 74.92, 74.04, 72.65, 68.71, 67.29, 66.96, 66.52, 66.40, 57.41, 55.30, 37.90, 29.45, 23.20, 16.42; ESI-MS: *m/z*: Calcd for $C_{54}H_{62}N_2NaO_{13}$ $[M+Na]^+$: 969.4, found 969.5.

3-([(Benzyloxy)carbonyl]amino)propyl (2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranoside (15). To a solution of **14** (2.20 g, 2.32 mmol) in MeCN (64 mL) and H_2O (10 mL) was added CAN (1.27 g, 2.32 mmol) at 0 °C. The reaction was stirred for 5 h at rt and then evaporated in vacuum to remove MeCN. The remaining aqueous solution was diluted with DCM (50 mL) and washed with satd aq $NaHCO_3$. The organic phase was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (DCM/MeOH, 0 to 20% MeOH) to afford **15** (1.43 g, 1.74 mmol, 74%) as an off-white solid.

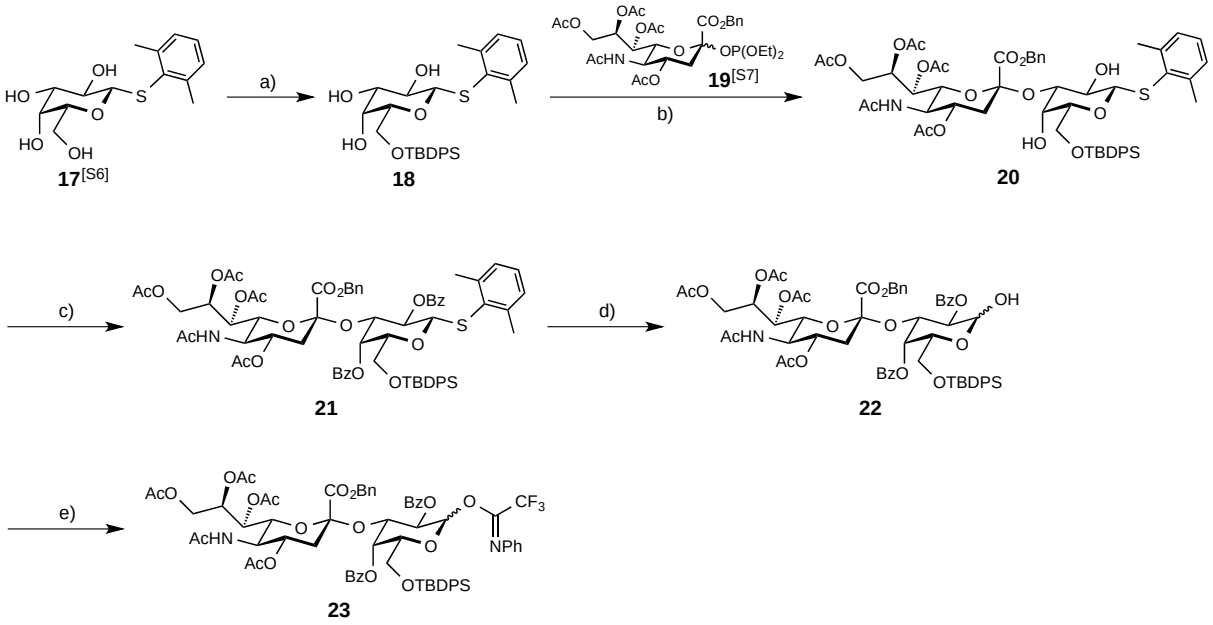
$[\alpha]_D^{20}$ -14.0 (*c* 0.10, acetone); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 (m, 20H), 5.83 (s, 1H), 5.28 (s, 1H), 5.10 (s, 2H), 4.96 (d, *J* = 11.4 Hz, 1H), 4.92 (s, 1H), 4.72 (m, 5H), 4.29 (s, 1H),

4.08 (m, 2H), 3.92 (m, 3H), 3.53 (m, 7H), 3.22 (s, 1H), 2.29 (m, 1H), 1.74 (m, 2H), 1.61 (s, 3H), 1.15 (d, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.28, 128.60, 128.53, 128.47, 128.37, 128.30, 128.04, 127.76, 127.68, 127.52, 100.89, 99.62, 84.95, 78.98, 76.14, 75.14, 75.03, 74.17, 73.02, 70.83, 68.29, 67.09, 66.59, 62.55, 55.33, 37.81, 29.48, 23.08, 16.67; ESI-MS: *m/z*: Calcd for $C_{46}H_{56}N_2NaO_{12}$ $[M+Na]^+$: 851.4, found 851.4.

3-([(Benzyloxy)carbonyl]amino)propyl (2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)-2-acetamido-2-deoxy-6-*O*-levulinyl-β-D-glucopyranoside (15). To a solution of **14** (365 mg, 0.441 mmol), DMAP (11 mg, 0.09 mmol) and levulinic acid (0.048 mL, 0.468 mmol) in DCM (5 mL) and DMF (1 mL) was added EDC (0.155 mL, 0.877 mmol) at -15 °C under argon. The reaction was stirred at 0 °C for 20 h and then quenched with satd aq NH_4Cl (20 mL). The mixture was extracted with DCM (3 × 20 mL), and the combined organic phases were dried over Na_2SO_4, filtered and evaporated in vacuum. The residue was purified by flash chromatography (DCM/MeOH, 0 to 10% MeOH) to afford **15** (270 mg, 0.291 mmol, 66%).

$[\alpha]_D^{20}$ -55.9 (*c* 1.00, acetone); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33 (m, 20H, Ar-H), 5.85 (d, J = 7.0 Hz, 1H, NH), 5.32 (bs, 1H, NH), 5.10 (m, 2H, Cbz), 4.96 (d, J = 11.4 Hz, 1H, CH_2Ph), 4.93 (d, J = 3.0 Hz, 1H, Fuc-H1), 4.81 (m, 2H, CH_2Ph), 4.75 (d, J = 11.8 Hz, 1H, CH_2Ph), 4.66 (m, 2H, Glc*N*Ac-H1, CH_2Ph), 4.62 (d, J = 11.5 Hz, 1H, CH_2Ph), 4.43 (d, J = 10.7 Hz, 1H, Glc*N*Ac-H6a), 4.25 (m, 2H, Glc*N*Ac-H6b, OH), 4.11 (m, 1H, Fuc-H5), 4.08 (dd, J = 10.2, 3.6 Hz, 1H, Fuc-H2), 3.94 (m, 1H, Fuc-H3), 3.91 (m, 1H, OCH_2), 3.68 (s, 1H, Fuc-H4), 3.62 (t, J = 9.2 Hz, 1H, Glc*N*Ac-H3), 3.52 (m, 1H, OCH_2), 3.46 (m, 2H, Glc*N*Ac-H2, -H5), 3.39 (m, 1H, NCH_2), 3.34 (t, J = 8.7 Hz, 1H, Glc*N*Ac-H4), 3.18 (m, 1H, NCH_2), 2.69 (t, J = 6.1 Hz, 2H, Lev), 2.58 (t, J = 6.4 Hz, 2H, Lev), 2.15 (s, 3H, Lev), 1.76 (m, 1H, CH_2), 1.71 (s, 1H, CH_2), 1.60 (s, 3H, $COCH_3$), 1.15 (d, J = 6.4 Hz, 3H, Fuc-H6); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 206.62 (CO), 172.63, 171.07 (2 CO), 156.65 (NCO), 138.55, 138.30, 136.88, 128.59, 128.52, 128.48, 128.38, 128.30, 128.03, 127.76, 127.53 (Ar-C), 100.66 (Glc*N*Ac-C1), 99.59 (Fuc-C1), 84.66, 79.01, 77.38, 76.16, 75.03 (*C*H_2Ph), 74.10 (*C*H_2Ph), 73.43, 73.03 (*C*H_2Ph), 70.36, 68.25 (Fuc-C5), 67.05 (OCH_2), 66.49 (Cbz), 63.68 (Glc*N*Ac-C6), 55.40, 37.89, 29.85, 29.53, 27.88, 23.10, 16.65 (Fuc-C6); ESI-MS: *m/z*: Calcd for $C_{51}H_{62}N_2NaO_{14}$ $[M+Na]^+$: 949.4, found 949.5.

Synthesis of Sia-Gal building block 23:



Scheme S4. a) TBDPSCl, pyridine, 0 °C to rt, 8 h (89%); b) TMSOTf, DCM/MeCN, MS 4Å, -72 °C, 5 h (64%); c) Bz_2O, DMAP, pyridine, rt, overnight (84%); d) NBS, pyridine, acetone/H_2O (12:1), 45 min (84%); e) trifluoro-*N*-phenylacetimidoyl chloride, K_2CO_3, acetone, 0 °C to rt, 2 h (96%).

2,6-Dimethylphenyl 6-*O*-(*tert*-butyldiphenylsilyl)-1-thio-β-D-galactopyranoside (18). To a suspension of 2,6-dimethylphenyl 1-thio-β-D-galactopyranoside (6) (**17**, 1.76 g, 7.86 mmol) and DMAP (42.0 mg, 0.344 mmol) in pyridine (15 mL) was added TBDPSCl (1.17 g, 4.25 mmol) at 0 °C under argon. After stirring for 8 h at rt the mixture was evaporated to dryness. The residue was dissolved in DCM (100 mL) and washed with brine (containing 1 N HCl) and satd aq $NaHCO_3$. The organic phase was dried with Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (petroleum ether/EtOAc + 10% MeOH, 0 to 50% EtOAc) to give **18** (1.85 g, 3.08 mmol, 89%) as a foam.

$[\alpha]_D^{20}$ -24.5 (*c* 2.00, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (dd, *J* = 10.6, 4.0 Hz, 4H), 7.42 (m, 6H), 7.18 (dd, *J* = 8.4, 6.5 Hz, 1H), 7.13 (d, *J* = 7.4 Hz, 2H), 4.27 (d, *J* = 9.8 Hz, 1H), 4.09 (d, *J* = 2.9 Hz, 1H), 3.87 (m, 2H), 3.78 (m, 1H), 3.56 (dd, *J* = 9.0, 3.3 Hz, 1H), 3.41 (t, *J* = 5.5 Hz, 1H), 2.83 (s, 3H), 2.58 (s, 6H), 1.06 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.06, 135.61, 135.54, 132.90, 132.82, 131.29, 129.89, 129.16, 128.30, 127.83, 91.30, 78.02, 74.95, 71.38, 69.06, 63.35, 26.78, 22.80, 19.13; ESI-MS: *m/z*: Calcd for $C_{30}H_{38}NaO_5SSi$ $[M+Na]^+$: 561.2, found 561.1.

2,6-Dimethylphenyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-6-*O*-(*tert*-butyldiphenylsilyl)-1-thio-β-D-galactopyranoside (20). Donor **19** (7) (420 mg, 0.569 mmol), acceptor **18** (170 mg, 0.316 mmol) and activated molecular sieves 4 Å (600 mg) were suspended in DCM/MeCN (1:1.2, 6 mL) under argon. The mixture was stirred for 1.5 h at rt and then cooled to -72 °C. TMSOTf (11.4 μL, 0.063 mmol) was added dropwise and the mixture was stirred at -72 °C for 5h. Then, the reaction was quenched with satd aq $NaHCO_3$ (5 mL) and filtered through celite. The celite was washed with DCM, and the filtrate was extracted with DCM (2 × 10 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (petroleum ether/EtOAc + 10% MeOH, 0 to 50% EtOAc, then DCM/MeOH, 0 to 20% MeOH) to yield **20** (219 mg, 0.201 mmol, 64%).

$[\alpha]_D^{20}$ +12.4 (*c* 1.00, acetone); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (m, 4H, Ar-H), 7.29 (m, 15H, Ar-H), 5.50 (ddd, *J* = 8.3, 5.2, 2.7 Hz, 1H Sia-H8), 5.36 (dd, *J* = 8.9, 1.5 Hz, 1H, Sia-H7), 5.22 (m, 2H, C*H*$_2$Ph, NH), 5.12 (d, *J* = 12.0 Hz, 1H, C*H*$_2$Ph), 4.94 (ddd, *J* = 12.3, 9.8, 4.5 Hz, 1H, Sia-H4), 4.48 (d, *J* = 9.7 Hz, 1H, Gal-H1), 4.27 (dd, *J* = 12.5, 2.6 Hz, 1H, Sia-H9a), 4.08 (m, 4H, Sia-H9b, Sia-H5, Sia-H6, Gal-H3), 3.82 (t, *J* = 9.4 Hz, 1H, Gal-H6a), 3.76 (dd, *J* = 10.5, 5.5 Hz, 1H, Gal-H2), 3.67 (dd, *J* = 10.5, 4.8 Hz, 1H, Gal-H6b), 3.59 (d, *J* = 2.9 Hz, 1H, Gal-H4), 3.32 (t, *J* = 5.2 Hz, 1H, Gal-H5), 2.84 (dd, *J* = 12.9, 4.5 Hz, 1H, Sia-H3*eq*), 2.61 (s, 6H, 2 Me), 2.17, 2.14 (2 s, 6H, 2 OAc), 2.08 (t, *J* = 12.5 Hz, 1H, Sia-H3*ax*), 2.06, 2.03 (2 s, 6H, 2 OAc), 1.92 (s, 3H, NAc), 1.05 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.75, 170.53, 170.26, 170.00, 169.89, 167.54, 144.40, 135.61, 134.19, 132.93, 132.88, 131.73, 129.86, 129.80, 128.94, 128.83, 128.77, 128.59, 127.99, 127.80, 127.76, 97.49, 90.25, 78.53, 72.76, 68.68, 68.52, 68.22, 66.89, 63.60, 62.15, 49.50, 38.08, 26.81, 23.20, 22.60, 21.24, 20.82, 20.74, 19.15; ESI-MS: *m/z*: Calcd for $C_{56}H_{69}NNaO_{17}SSi$ $[M+Na]^+$: 1110.4, found 1110.5.

2,6-Dimethylphenyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-2,4-di-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-1-thio-β-D-galactopyranoside (21). A solution of **20** (1.22 g, 1.13 mmol), DMAP (750 mg), and Bz_2O (895 mg, 3.96 mmol) in dry pyridine (8 mL) was stirred overnight at rt under argon. The solvents were co-evaporated twice with xylene at 30 °C. The residue was diluted with brine (50 mL, contained 0.1 N HCl) and extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with satd aq $NaHCO_3$, dried over Na_2SO_4, filtered and

concentrated. The residue was purified by flash chromatography (petroleum ether/EtOAc + 20% MeOH, 0 to 50% EtOAc) to yield **21** (1.23 g, 0.95 mmol, 84%) as a white solid. $[\alpha]_D^{20}$ +75.6 (*c* 1.00, acetone); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 7.3 Hz, 2H, Ar-H), 8.07 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.59 (m, 4H, Ar-H), 7.48 (m, 8H, Ar-H), 7.39 (m, 6H, Ar-H), 7.25 (m, 1H, Ar-H), 7.08 (m, 3H, Ar-H), 7.02 (d, *J* = 7.5 Hz, 2H, Ar-H), 5.76 (d, *J* = 2.9 Hz, 1H, Gal-H4), 5.67 (m, 1H, Sia-H8), 5.50 (d, *J* = 12.1 Hz, 1H, C*H*$_2$Ph), 5.06 (m, 1H, Gal-H2), 5.28 (d, *J* = 12.1 Hz, 1H, C*H*$_2$Ph), 5.16 (dd, *J* = 9.9, 2.8 Hz, 1H, Sia-H7), 4.97 (dd, *J* = 9.6, 2.6 Hz, 1H, Gal-H3), 4.93 (d, *J* = 10.0 Hz, 1H, Gal-H1), 4.89 (m, 1H, Sia-H4), 4.75 (d, *J* = 10.2 Hz, 1H, NH), 4.35 (dd, *J* = 12.3, 2.1 Hz, 1H, Sia-H9a), 3.98 (dd, *J* = 12.4, 6.1 Hz, 1H, Sia-H9b), 3.85 (t, *J* = 7.2 Hz, 1H, Gal-H5), 3.80 (q, *J* = 10.6 Hz, 1H, Sia-H5), 3.61 (m, 2H, Gal-H6), 3.40 (dd, *J* = 10.8, 2.8 Hz, 1H, Sia-H6), 2.51 (dd, *J* = 12.6, 4.7 Hz, 1H, Sia-H3*eq*), 2.42 (s, 6H, 2 Me), 2.20, 2.06, 1.90, 1.75 (4 s, 12H, 4 OAc), 1.64 (t, *J* = 12.4 Hz, 1H, Sia-H3*ax*), 1.49 (s, 3H, NAc), 1.04 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.66, 170.58, 170.51, 170.26, 170.20, 170.15, 167.68, 165.59, 165.39 (CO), 144.28, 135.61, 135.50, 135.24, 133.07, 133.01, 132.91, 132.84, 131.16, 130.52, 130.05, 129.78, 129.60, 129.02, 128.85, 128.58, 128.55, 128.53, 128.47, 128.32, 128.06, 127.79, 127.76, 127.57, 127.54 (Ar-C), 96.94, 87.85, 77.39, 77.13, 76.88, 76.62, 73.09, 71.67, 70.45, 69.76, 68.51, 68.20, 67.40, 66.55, 62.63, 60.79, 48.65, 37.35, 26.78, 26.75, 23.15, 22.63, 22.61, 21.53, 20.82, 20.75, 20.49, 19.12; ESI-MS: *m/z*: Calcd for $C_{70}H_{77}NNaO_{19}SSi$ $[M+Na]^+$: 1318.5, found 1318.6.

(Benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulo-pyranosynate)-(2→3)-2,4-di-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-α- and β-D-galacto-pyranoside (22). To a solution of **21** (870 mg, 0.671 mmol) and pyridine (120 mg, 1.5 mmol) in acetone (12 mL) and H_2O (1 mL) was added NBS (1.78 g, 10.0 mmol) during 3 min at rt. The solution turned orange and after 45 min TLC (DCM/acetone, 4:1) showed complete conversion. The reaction was quenched by addition of satd aq $NaHCO_3$ (30 mL), $Na_2S_2O_3$ (3 g) and H_2O (10 mL). Acetone was evacuated under reduced pressure and the residue diluted with HCl in brine (80 mL, 0.1 N HCl) and extracted with EtOAc (2 × 100 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (petroleum ether/acetone, 0 to 50% acetone) to give **22** (665 mg, 0.565 mmol, 84%) as an off-white solid. Surprisingly, the α- and β-isomer were separated on column, and were stable in $CDCl_3$ for 1 d.

α-Isomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (m, 2H, Ar-H), 8.05 (d, *J* = 7.1 Hz, 2H, Ar-H), 7.50 (m, 18H, Ar-H), 7.24 (d, *J* = 7.5 Hz, 1H, Ar-H), 7.08 (t, *J* = 7.6 Hz, 2H, Ar-H), 5.85

(d, *J* = 2.8 Hz, 1H, Gal-H4), 5.67 (ddd, *J* = 8.7, 6.2, 2.3 Hz, 1H, Sia-H8), 5.55 (d, *J* = 12.1 Hz, 1H, C*H*$_2$Ph), 5.51 (dd, *J* = 10.8, 3.9 Hz, 1H, Gal-H2), 5.45 (dd, *J* = 8.0, 3.9 Hz, 1H, Gal-H1), 5.33 (d, *J* = 12.1 Hz, 1H, C*H*$_2$Ph), 5.27 (dd, *J* = 9.1, 2.9 Hz, 1H, Sia-H7), 5.17 (dd, *J* = 10.8, 3.1 Hz, 1H, Gal-H3), 4.93 (m, 1H, Sia-H4), 4.93 (s, 1H, NH), 4.57 (d, *J* = 8.1 Hz, 1H, Gal-1-OH), 4.40 (dd, *J* = 8.9, 5.6 Hz, 1H, Gal-H5), 4.34 (dd, *J* = 12.4, 2.3 Hz, 1H, Sia-H9a), 4.03 (dd, *J* = 12.4, 6.2 Hz, 1H, Sia-H9b), 3.97 (q, *J* = 10.5 Hz, 1H, Sia-H5), 3.70 (dd, *J* = 9.7, 5.4 Hz, 1H, Gal-H6a), 3.65 (t, *J* = 9.4 Hz, 1H, Gal-H6b), 3.47 (dd, *J* = 10.8, 3.0 Hz, 1H, Sia-H6), 2.55 (dd, *J* = 12.6, 4.7 Hz, 1H, Sia-H3*eq*), 2.28, 2.07, 1.91, 1.79 (4 s, 12H, 4 OAc), 1.69 (s, 3H, NAc), 1.65 (t, *J* = 12.4 Hz, 1H, Sia-H3*ax*), 1.06 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (126 MHz, CDCl_3): δ = 171.73, 171.00, 170.65, 170.28, 170.21, 167.69, 165.95, 165.43 (CO), 135.59, 135.46, 135.13, 133.20, 132.99, 132.87, 132.81, 130.23, 130.01, 129.94, 129.78, 129.56, 129.05, 128.59, 128.51, 128.42, 127.75, 127.52 (Ar-C), 97.20 (Sia-C2), 92.17 (Gal-C1), 72.11, 70.16, 69.59, 69.02, 68.70, 68.62, 68.45, 68.39, 66.73, 62.66 (Sia-C9), 60.93 (Gal-C6), 48.77, 37.30, 26.75, 23.12, 21.63, 20.78, 20.70, 19.13; ESI-MS: *m/z*: Calcd for $C_{62}H_{69}NNaO_{20}Si$ $[M+Na]^+$: 1198.4, found: 1198.5.

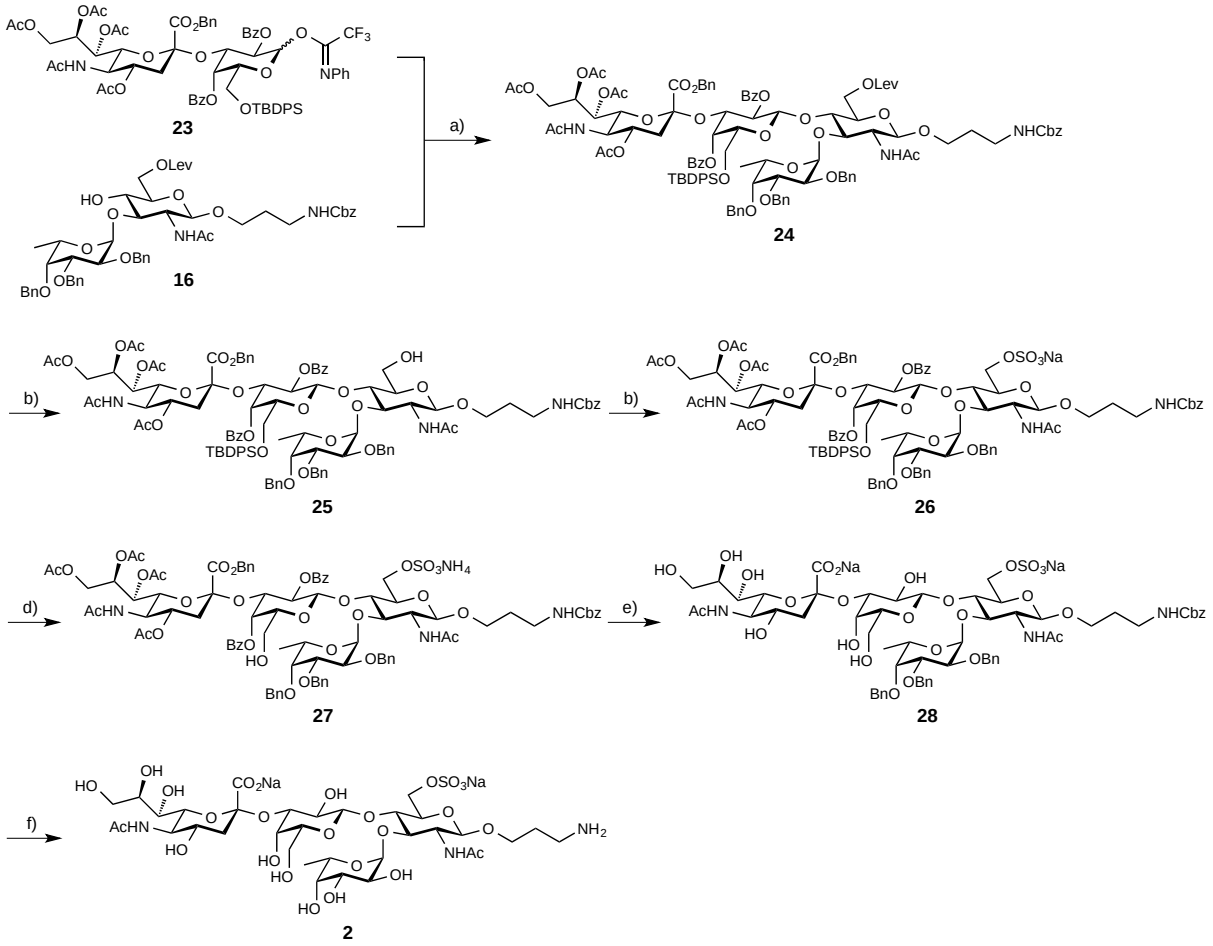
β-Isomer: ^{1}H NMR (500 MHz, CDCl_3): δ = 8.20 (m, 2H, Ar-H), 8.03 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.66 (m, 2H, Ar-H), 7.58 (t, *J* = 7.4 Hz, 2H, Ar-H), 7.51 (m, 6H, Ar-H), 7.40 (m, 8H, Ar-H), 7.26 (m, 1H, Ar-H), 7.09 (t, *J* = 7.6 Hz, 2H, Ar-H), 5.84 (d, *J* = 2.8 Hz, 1H, Gal-H4), 5.65 (ddd, *J* = 9.2, 5.3, 2.5 Hz, 1H, Sia-H8), 5.52 (d, *J* = 12.1 Hz, 1H, C*H*$_2$Ph), 5.34 (d, *J* = 12.4 Hz, 1H, C*H*$_2$Ph), 5.32 (dd, *J* = 9.7, 2.5 Hz, 1H, Sia-H7), 5.20 (dd, *J* = 10.2, 8.0 Hz, 1H, Gal-H2), 5.09 (dd, *J* = 10.3, 3.1 Hz, 1H, Gal-H3), 5.04 (t, *J* = 8.2 Hz, 1H, Gal-H1), 4.95 (m, 1H, Sia-H4), 4.92 (d, *J* = 10.3 Hz, 1H, NH), 4.34 (dd, *J* = 12.4, 2.4 Hz, 1H, Sia-H9a), 4.10 (dd, *J* = 9.0, 5.6 Hz, 1H, Gal-H5), 4.04 (dd, *J* = 11.1, 3.7 Hz, 1H, Sia-H9b), 4.00 (t, *J* = 9.0 Hz, 1H, Sia-H5), 3.76 (d, *J* = 8.5 Hz, 1H, Gal-1-OH), 3.75 (dd, *J* = 9.6, 5.7 Hz, 1H, Gal-H6a), 3.68 (t, *J* = 9.5 Hz, 1H, Gal-H6b), 3.51 (dd, *J* = 10.8, 2.8 Hz, 1H, Sia-H6), 2.54 (dd, *J* = 12.6, 4.7 Hz, 1H, Sia-H3*eq*), 2.23, 2.08, 1.91, 1.80 (4 s, 12H, 4 OAc), 1.65 (t, *J* = 12.5 Hz, 1H, Sia-H3*ax*), 1.60 (s, 3H, NAc), 1.07 (s, 9H, C(CH_3)$_3$); ^{13}CNMR (126 MHz, CDCl_3): δ = 170.72, 170.65, 170.57, 170.30, 170.10, 167.53, 167.46, 165.35 (CO), 135.57, 135.45, 133.42, 132.99, 132.76, 130.31, 129.95, 129.76, 129.58, 128.98, 128.57, 128.53, 128.39, 127.74, 127.53 (Ar-C), 97.03 (Sia-C2), 96.06 (Gal-C1), 73.87, 73.33, 72.02, 71.30, 69.61, 68.60, 67.93, 67.60, 66.62, 62.31 (Sia-C9), 60.70 (Gal-C6), 48.86, 37.41, 26.73, 23.14, 21.54, 20.82, 20.70, 19.12; ESI-MS: *m/z*: Calcd for $C_{62}H_{69}NNaO_{20}Si$ $[M+Na]^+$: 1198.4, Found: 1198.6.

(Benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulo-pyranosynate)-(2→3)-2,4-di-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-D-galactopyranosyl

trifluoro-*N*-phenylacetimidate (23). To a suspension of **22** (665 mg, 0.565 mmol) and K_2CO_3 (350 mg, 2.54 mmol) in acetone (4 mL) was added dropwise trifluoro-*N*-phenylacetimidoyl chloride (0.25 mL, 1.55 mmol) at 0 °C under argon. The mixture was allowed to warm to rt and stirred for 2 h. DCM (50 mL) was added and the mixture was filtered through celite. The filtrate was concentrated and the residue was purified by flash chromatography (petroleum ether/acetone, 20 to 60% acetone) to give **23** (727 mg, 0.540 mmol, 96%, α/β = 1:1) as off-white foam.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.26-8.14 (m, 2H), 8.06 (d, *J* = 7.6 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.77-6.93 (m, 25H, Ar-H), 6.76 (d, *J* = 6.6 Hz, 0.5 H), 6.44 (d, *J* = 6.3 Hz, 0.5 H), 5.99 (s, 0.5 H), 5.79 (s, 0.5 H), 5.66 (m, 1H), 5.53 (m, 2.5 H), 5.44 (d, *J* = 9.7 Hz, 0.5 H), 5.37 (d, *J* = 12.2 Hz, 0.5 H), 5.32 (d, *J* = 12.1 Hz, 0.5 H), 5.15 (d, *J* = 9.6 Hz, 0.5 H), 5.10 (b, 0.5 H), 5.02 (d, *J* = 10.3 Hz, 0.5 H), 4.91 (m, 1H), 4.85 (d, *J* = 10.3 Hz, 0.5 H), 4.70 (s, 0.5 H), 4.36 (d, *J* = 12.1 Hz, 0.5 H), 4.27 (d, *J* = 12.4 Hz, 0.5 H), 4.16 (dd, *J* = 12.3, 2.8 Hz, 0.5 H), 4.10 (q, *J* = 10.4 Hz, 0.5 H), 3.91 (dd, *J* = 12.2, 6.5 Hz, 0.5 H), 3.83 (q, *J* = 10.5 Hz, 0.5 H), 3.67 (m, 2.5 H), 3.45 (d, *J* = 10.7 Hz, 0.5 H), 2.57 (m, 1H), 2.22 (s, 1.5 H), 2.16 (s, 1.5 H), 2.06 (s, 1.5 H), 1.96 (s, 1.5 H), 1.91 (s, 5H), 1.85 (s, 1.5 H), 1.76 (s, 1.5 H), 1.66 (t, *J* = 12.4 Hz, 0.5 H), 1.64 (t, *J* = 12.4 Hz, 0.5 H), 1.43 (s, 1.5 H), 1.09 (s, 4.5 H), 1.07 (s, 4.5 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.74, 170.67, 170.59, 170.50, 170.33, 170.22, 170.17, 169.88, 169.49, 167.60, 167.48, 165.96, 165.42, 165.24, 165.08, 143.39, 135.69, 135.67, 135.51, 135.49, 135.41, 135.15, 133.62, 133.22, 133.10, 133.05, 132.92, 132.82, 132.74, 130.23, 130.08, 130.06, 129.91, 129.86, 129.73, 129.66, 129.61, 129.58, 128.98, 128.79, 128.76, 128.59, 128.56, 128.53, 128.49, 128.46, 127.78, 127.74, 127.59, 124.25, 124.01, 119.50, 119.14, 96.88, 96.83, 74.22, 72.34, 72.06, 71.80, 71.63, 70.76, 69.59, 69.54, 68.92, 68.63, 68.58, 68.51, 68.08, 67.61, 67.54, 67.35, 66.66, 66.61, 62.71, 61.87, 61.04, 60.66, 49.14, 48.66, 38.03, 37.24, 26.76, 23.22, 23.12, 21.53, 21.39, 20.86, 20.76, 20.73, 20.60, 20.26, 19.20, 19.15, 17.53.

Synthesis of 6-sulfo sialyl Lewis^x (2):



Scheme S5. a) TMSOTf, MS 4 Å, -18 °C to rt, 2 d (36%); b) H_2N-NH_2·HOAc, EtOH, overnight, rt (83%); c) SO_3-pyr, DMF, 40 min (67%); d) HF-pyr, pyridine, rt, 1 h (86%); e) NaOMe, MeOH, 8 h (90%); f) H_2, $Pd(OH)_2$/C, H_2O/MeOH, 16 h (60%).

3-([(Benzyloxy)carbonyl]amino)propyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-[2,4-di-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-galactopyranosyl]-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-6-*O*-levulinyl-β-D-glucopyranoside (24). Donor **23** (725 mg, 0.539 mmol), acceptor **16** (450 mg, 0.485 mmol) and activated molecular sieves 4 Å (760 mg) were suspended in dry DCM (8 mL) under argon. The mixture was stirred for 1.5 h at rt and then cooled to -18 °C. TMSOTf (10 µL, 0.055 mmol) was added dropwise and the reaction mixture was allowed to warm to 18 °C overnight. Then, the mixture was cooled to -12 °C, TMSOTf (10 µL, 0.055 mmol) was added dropwise, and the mixture was allowed to warm to rt during 20 h. The reaction then was quenched with NEt_3 (100 µL) and filtered through celite. The celite was washed with DCM and the filtrate was

concentrated. The residue was purified by flash chromatography (DCM/MeOH, 0 to 20% MeOH) to yield **24** (358 mg, 0.172 mmol, 36%) as a white solid.

$[\alpha]_D^{20}$ +0.25 (*c* 1.00, DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 7.6 Hz, 2H, Ar-H), 8.04 (d, *J* = 7.6 Hz, 2H, Ar-H), 7.38 (m, 39H, Ar-H), 7.00 (t, *J* = 7.3 Hz, 2H, Ar-H), 6.19 (d, *J* = 7.9 Hz, 1H, NH), 5.86 (s, 1H, Gal-H4), 5.67 (d, *J* = 9.3 Hz, 1H), 5.52 (d, *J* = 12.1 Hz, 1H), 5.39 (t, *J* = 9.0 Hz, 1H, Gal-H2), 5.31 (d, *J* = 12.2 Hz, 2H), 5.07 (m, 5H, Glc*N*Ac-H1, Gal-H3, C*H*$_2$Ph), 4.92 (td, *J* = 11.4, 4.1 Hz, 1H, Sia-H4), 4.83 (dd, *J* = 11.8, 5.7 Hz, 3H), 4.64 (s, 2H), 4.54 (d, *J* = 11.2 Hz, 1H), 4.42 (m, 4H), 4.30 (dd, *J* = 11.1, 5.9 Hz, 1H), 3.90 (m, 11H), 3.53 (m, *J* = 15.9 Hz, 3H), 3.46 (d, *J* = 10.6 Hz, 1H), 3.08 (m, 3H), 2.66 (m, 2H, OCH_2), 2.55 (m, 3H, CH_2CO, Sia-H3*eq*), 2.24 (s, 3H, OAc), 2.08 (s, 3H, Me), 2.09, 1.89, 1.86, 1.77 (4 s, 12H, 4 OAc), 1.62 (t, *J* = 12.2 Hz, 1H, Sia-H3*ax*), 1.58 (s, 3H, NAc), 1.47 (m, 2H, CH_2), 1.06 (s, 9H, $C(CH_3)_3$), 0.98 (d, *J* = 5.9 Hz, 3H, Fuc-H6); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 206.35, 172.28, 170.79, 170.61, 170.53, 170.24, 169.99, 167.60, 165.91, 165.67 (CO), 156.51 (NCO), 138.90, 138.77, 138.59, 135.48, 135.35, 135.14, 133.33, 133.09, 132.79, 132.50, 130.19, 130.06, 129.87, 129.67, 128.97, 128.57, 128.51, 128.43, 128.29, 128.17, 128.10, 128.01, 127.92, 127.86, 127.58, 127.42, 127.28 (Ar-C), 100.53, 99.86, 96.89, 96.74, 79.15, 78.18, 76.33, 74.91, 73.85, 73.64, 73.41, 73.00, 72.83, 72.71, 71.74, 71.41, 69.69, 68.59, 67.89, 67.42, 66.98, 66.33, 66.27, 66.19, 63.67, 61.99, 60.44, 52.50, 48.73, 37.70, 37.23, 29.75, 29.19, 27.75, 26.71, 23.16, 21.62, 20.83, 20.71, 20.56, 19.13, 16.63; ESI-MS: *m/z*: Calcd for $C_{113}H_{129}N_3Na_2O_{33}Si$ $[M+2Na]^{2+}$: 1064.9, found 1065.7.

3-([(Benzyloxy)carbonyl]amino)propyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-[2,4-di-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-galactopyranosyl]-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-β-D-glucopyranoside (25). Compound **24** (65 mg, 31 µmol) was treated with anhydrous hydrazine acetate salt (4.3 mg, 47 µmol) in dry EtOH (1.0 mL) overnight at rt under argon. Then AcOH (20 mg, 333 µmol) was added and after 5 min toluene (5 mL) was added. The solvents were evaporated in vacuum and the residue was purified by flash chromatography (petroleum ether/EtOAc + 10% MeOH, 0 to 100% EtOAc) to yield **25** (51 mg, 26 µmol, 83%) as an off-white glassy solid.

$[\alpha]_D^{20}$ -1.63 (*c* 1.00, DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 7.2 Hz, 2H), 8.09-7.99 (m, 2H), 7.63 (d, *J* = 6.7 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.50 (m, 5H), 7.45-6.90 (m, 33H), 6.00 (d, *J* = 8.4 Hz, 1H), 5.82 (d, *J* = 3.1 Hz, 1H), 5.77 (t, *J* = 7.7 Hz, 1H), 5.53 (d, *J* = 12.1 Hz, 1H), 5.43 (m, 1H), 5.39 (dd, *J* = 10.2, 8.1 Hz, 1H), 5.30 (d, *J* = 12.0 Hz, 1H), 5.21-5.10 (m, 2H), 5.04 (m, 2H), 4.99 (dd, *J* = 10.3, 2.8 Hz, 1H), 4.95-4.76 (m, 4H), 4.64 (s, 2H),

4.51-4.43 (m, 2H), 4.38 (m, 2H), 4.16 (m, 2H), 4.00-3.65 (m, 12H), 3.55 (m, 1H), 3.49 (d, *J* = 1.5 Hz, 1H), 3.42 (dd, *J* = 10.7, 2.4 Hz, 1H), 3.31 (m, 1H), 3.24-2.96 (m, 3H), 2.50 (dd, *J* = 12.6, 4.7 Hz, 1H), 2.25 (s, 3H), 2.08 (s, 3H), 1.90 (s, 3H), 1.79 (s, 3H), 1.76 (s, 3H), 1.67-1.45 (m, 2H), 1.63 (t, *J* = 12.4 Hz, 1H), 1.54 (s, 3H), 1.06 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.72, 170.65, 170.57, 170.30, 170.10, 167.53, 167.46, 165.35, 135.57, 135.45, 133.42, 132.99, 132.76, 130.31, 129.95, 129.76, 129.58, 128.98, 128.57, 128.53, 128.39, 127.74, 127.53, 97.03, 96.06, 73.87, 73.33, 72.02, 71.30, 69.61, 68.60, 67.93, 67.60, 66.62, 62.31, 60.70, 48.86, 37.41, 26.73, 23.14, 21.54, 20.82, 20.70, 19.12; ESI-MS: *m/z*: Calcd for $C_{108}H_{123}N_3NaO_{31}Si$ $[M+Na]^+$: 2008.8, found: 2009.1.

3-([(Benzyloxy)carbonyl]amino)propyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-[2,4-di-*O*-benzoyl-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-galactopyranosyl]-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-6-*O*-sulfo-β-D-glucopyranoside sodium salt (26). To a solution of **25** (37 mg, 18.6 µmol) in DMF (0.4 mL) was added SO_3-pyridine (37 mg, 233 µmol) at 0 °C under argon and the mixture was stirred at rt for 40 min. Then, fine powdered $NaHCO_3$ (120 mg, 1.43 mmol) was added stirring was continued for 1 h. The mixture was diluted with DCM (5 mL) and filtered through celite. The celite was washed with DCM/MeOH (5:1, 40 mL), the filtrate was concentrated and co-evaporated with xylene. The residue was purified by flash chromatography (DCM/MeOH, 0 to 20% MeOH) to yield **26** (26 mg, 12.4 µmol, 67%) as an off-white glassy solid.

$[\alpha]_D^{20}$ -6.07 (*c* 1.00, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 7.4 Hz, 2H), 8.05 (d, *J* = 7.6 Hz, 2H), 7.38 (m, 40H), 6.39 (d, *J* = 9.4 Hz, 1H), 5.86 (d, *J* = 2.6 Hz, 1H), 5.76 (t, *J* = 7.3 Hz, 1H), 5.53 (d, *J* = 12.1 Hz, 1H), 5.33 (m, 2H), 5.19 (d, *J* = 8.5 Hz, 1H), 5.11 (m, 2H), 4.98 (m, 3H), 4.75 (m, 6H), 4.50 (m, 2H), 4.32 (d, *J* = 11.3 Hz, 1H), 4.22 (d, *J* = 8.5 Hz, 1H), 4.15 (d, *J* = 9.5 Hz, 1H), 3.96 (m, 8H), 3.69 (m, 3H), 3.63 (t, *J* = 9.6 Hz, 1H), 3.44 (d, *J* = 11.6 Hz, 1H), 3.31 (m, 1H), 3.05 (m, 1H), 2.82 (m, 1H), 2.51 (dd, *J* = 12.0, 4.2 Hz, 1H), 2.42 (m, 1H), 2.25 (s, 3H), 2.13 (s, 3H), 2.07 (s, 3H), 1.89 (s, 3H), 1.77 (s, 3H), 1.63 (t, *J* = 12.3 Hz, 1H), 1.58 (s, 3H), 1.49 (m, 1H), 1.28 (m, 1H), 1.09 (s, 9H), 0.85 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.31, 169.91, 169.60, 169.35, 169.05, 166.51, 166.18, 164.35, 155.95, 138.10, 137.58, 136.04, 135.40, 134.56, 134.38, 134.17, 132.68, 132.08, 131.64, 131.48, 129.37, 128.91, 128.89, 128.58, 128.08, 127.97, 127.79, 127.58, 127.46, 127.25, 127.18, 127.03, 126.89, 126.69, 126.51, 126.27, 102.60, 98.18, 95.90, 95.59, 77.76, 74.73, 74.34, 73.87, 73.49, 72.25, 71.57, 70.80, 70.74, 70.43, 69.69, 68.59, 67.61, 66.70, 66.62, 66.31, 66.21, 66.07, 65.77, 62.11, 59.19, 51.29, 47.44, 36.14, 35.72, 29.51, 28.67,

25.78, 21.98, 21.92, 20.45, 19.88, 19.68, 19.56, 18.12, 15.46; ESI-MS: *m/z*: Calcd for $C_{108}H_{122}N_3O_{34}SSi$ $[M-Na]^-$: 2064.7, found: 2065.4.

3-([(Benzyloxy)carbonyl]amino)propyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-(2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-6-*O*-sulfo-β-D-glucopyranoside ammonium salt (27). Compound **26** (26 mg, 12.6 μmol) was treated in a Teflon flask with a solution of HF-pyridine (0.2 mL) in pyridine (0.6 mL) for 1 h at rt. The mixture was added to satd aq NH_4Cl (10 mL) and extracted with DCM (7 × 20 mL). The combined organic phases were dried with Na_2SO_4, and evaporated in vacuum. The residue was purified by flash chromatography (DCM/MeOH, 0 to 20% MeOH) to yield **27** (20 mg, 10.8 μmol, 86%) as a white glassy solid.
$[\alpha]_D^{20}$ -22.5 (*c* 1.00, MeOH); ^{1}H NMR (500 MHz, CD_3OD): δ = 8.32 (d, *J* = 7.2 Hz, 2H), 8.05 (m, 2H), 7.67 (t, *J* = 7.3 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.24 (m, 25H), 5.55 (dd, *J* = 9.7, 8.4 Hz, 1H), 5.44 (ddd, *J* = 7.7, 5.2, 2.5 Hz, 1H), 5.41 (d, *J* = 3.5 Hz, 1H), 5.33 (d, *J* = 3.5 Hz, 1H), 5.29 (m, 2H), 5.16 (d, *J* = 12.3 Hz, 1H), 5.07 (m, 3H), 4.78 (m, 3H), 4.60 (d, *J* = 11.2 Hz, 1H), 4.51 (m, 2H), 4.40 (dd, *J* = 10.6, 4.3 Hz, 1H), 4.35 (d, *J* = 8.1 Hz, 1H), 4.33 (d, *J* = 7.9 Hz, 1H), 4.29 (dd, *J* = 10.4, 1.9 Hz, 1H), 4.17 (m, 2H), 4.11 (m, 1H), 4.05 (t, *J* = 8.8 Hz, 2H), 3.83 (m, 10H), 3.36 (m, 1H), 3.21 (m, 1H), 3.11 (m, 1H), 2.36 (dd, *J* = 12.7, 4.7 Hz, 1H), 2.09 (s, 3H), 2.05 (s, 3H), 1.98 (d, *J* = 7.0 Hz, 2H), 1.90 (s, 2H), 1.89 (s, 3H), 1.83 (t, *J* = 12.4 Hz, 1H), 1.78 (s, 3H), 1.68 (m, 2H), 1.39 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, CD_3OD): δ = 173.33, 172.67, 171.69, 171.57, 168.73, 168.37, 167.03, 158.88, 140.25, 140.02, 139.42, 136.14, 134.81, 134.65, 131.68, 131.44, 131.18, 130.95, 130.16, 130.03, 129.66, 129.55, 129.48, 129.28, 129.17, 129.12, 128.94, 128.77, 128.70, 128.45, 128.40, 128.27, 102.89, 101.41, 101.27, 99.33, 97.50, 80.54, 79.93, 76.82, 76.39, 75.37, 75.09, 74.94, 73.81, 73.57, 73.12, 72.87, 72.73, 70.76, 70.62, 69.03, 68.52, 67.92, 67.32, 66.71, 63.26, 63.04, 56.88, 38.60, 37.87, 30.81, 23.46, 22.64, 21.28, 20.97, 20.64, 17.31; ESI-MS: *m/z*: Calcd for $C_{92}H_{104}N_3Na_2O_{34}S$ $[M+Na]^+$: 1872.6, found: 1872.8.

3-([(Benzyloxy)carbonyl]amino)propyl (5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-(β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-6-*O*-sulfo-β-D-glucopyranoside disodium salt (28). A solution of **27** (16 mg, 8.7 μmol) in MeOH (0.3 mL) was treated with 1.5 N NaOMe/MeOH (0.3 mL, 450 μmol) for 8 h at rt under argon. The mixture was

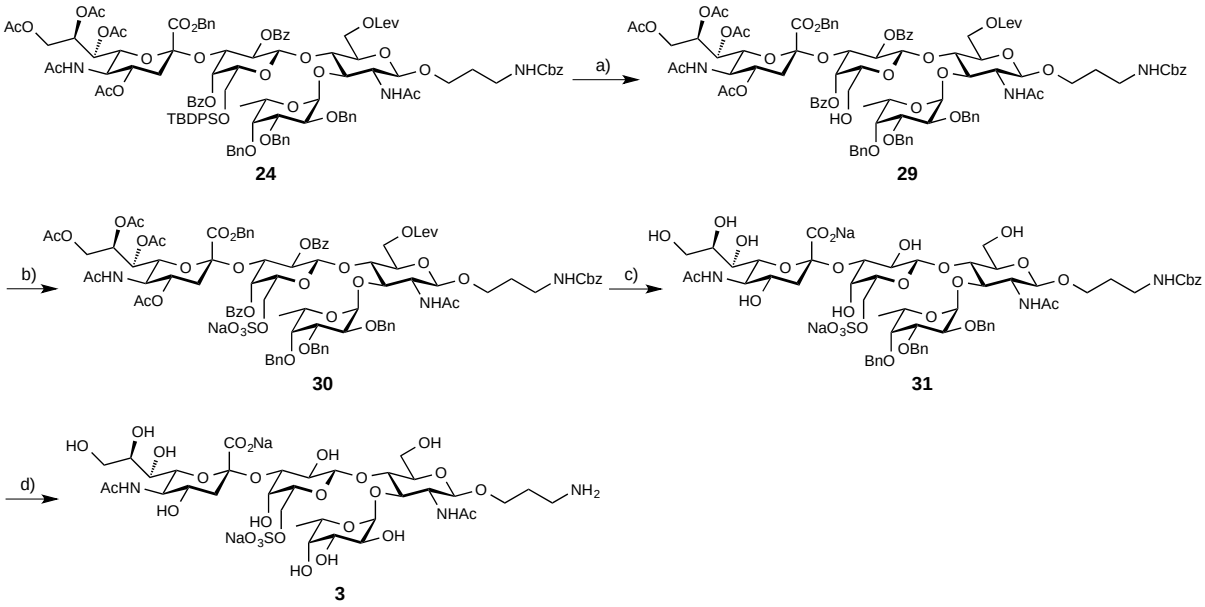
then neutralized with 1 N methanolic HCl pH 7-8 and concentrated. The residue was purified by reversed-phase chromatography on RP18 (MeCN/H_2O, 0 to 100% MeCN) to yield **28** (11 mg, 7.8 µmol, 90%) as an off-white glassy solid.

^{1}H NMR (500 MHz, D_2O): δ = 7.34 (m, 20H), 5.34 (d, *J* = 3.2 Hz, 1H), 5.04 (d, *J* = 12.5 Hz, 2H), 4.71 (m, 1H), 4.60 (m, 6H), 4.44 (d, *J* = 11.4 Hz, 1H), 4.38 (d, *J* = 7.0 Hz, 1H), 4.30 (m, 2H), 4.02 (dd, *J* = 9.8, 3.2 Hz, 1H), 3.97 (m, 2H), 3.85 (m, 10H), 3.59 (m, 10H), 3.44 (dd, *J* = 9.7, 8.0 Hz, 1H), 3.08 (dt, *J* = 12.7, 6.3 Hz, 2H), 2.70 (dd, *J* = 12.4, 4.6 Hz, 1H), 1.97 (s, 3H), 1.89 (s, 3H), 1.75 (t, *J* = 12.1 Hz, 1H), 1.65 (m, 2H), 1.07 (d, *J* = 6.5 Hz, 3H); ESI-MS: *m/z*: Calcd for $C_{63}H_{81}N_3O_{28}S$, $[M-2Na]^{2-}$: 679.7, found: 679.8.

3-Aminopropyl 6-sulfo sialyl Lewis^x disodium salt (2). A suspension of **28** (11 mg, 7.8 µmol) and $Pd(OH)_2/C$ (10 mg, 20% Pd) in MeOH/H_2O (2:1, 1 mL) was hydrogenated (50 bar H_2) in a Parr Shaker for 16 h. Then, the mixture was filtered through celite, and the celite was washed with MeOH/H_2O. The filtrate was concentrated and the residue was purified by flash chromatography (DCM/MeOH/H_2O, 100:49:11 to 0:45:10) followed by reversed-phase chromatography on RP18 (pure water) to yield **2** (8) (4.6 mg, 4.6 µmol, 60%) as an off-white glassy solid.

^{1}H NMR (500 MHz, D_2O): δ = 5.05 (d, *J* = 4.0 Hz, 1H), 4.74 (m, 1H), 4.54 (d, *J* = 7.8 Hz, 1H), 4.49 (t, *J* = 10.5 Hz, 1H), 4.32 (d, *J* = 2.6 Hz, 2H), 4.03 (dd, *J* = 9.8, 3.1 Hz, 1H), 3.74 (m, 12H), 3.46 (m, 8H), 3.04 (t, *J* = 6.8 Hz, 2H), 2.69 (dd, *J* = 12.4, 4.6 Hz, 1H), 1.97 (s, 6H), 1.89 (m, 2H), 1.73 (t, *J* = 12.1 Hz, 1H), 1.11 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, D_2O): δ = 174.97, 174.40, 174.01, 101.23, 101.04, 99.60, 98.51, 75.43, 74.87, 74.64, 72.88, 72.83, 72.61, 71.88, 71.39, 69.39, 69.17, 68.41, 68.30, 68.05, 67.72, 67.27, 66.73, 65.91, 62.55, 61.51, 55.55, 51.72, 39.71, 37.83, 26.66, 22.17, 22.03, 15.27; ESI-MS: *m/z*: Calcd for $C_{34}H_{57}N_3NaO_{26}S$ $[M-Na]^-$: 978.3, found: 978.6.

Synthesis of 6′-sulfo sialyl Lewis^x (3):



Scheme S6. a) HF-pyr, pyridine, rt, 1 h (91%); b) SO_3-pyr, DMF, 2 h (85%); c) NaOMe, MeOH, overnight (90%); d) H_2, $Pd(OH)_2$/C, H_2O/MeOH, 24 h (49%).

3-([(Benzyloxy)carbonyl]amino)propyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-(2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-6-*O*-levulinyl-β-D-glucopyranoside (29). According to the procedure for **27**, compound **24** (146 mg, 700 µmol) was treated with HF-pyridine (0.33 mL) in pyridine (1.0 mL) for 1 h at rt to yield **29** (118 mg, 639 µmol, 91%) as a white glassy solid.
$[\alpha]_D^{20}$ -7.78 (*c* 1.00, DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 7.3 Hz, 2H), 8.03 (m, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.51 (m, 3H), 7.42 (m, 2H), 7.26 (m, 25H), 6.08 (d, *J* = 8.4 Hz, 1H), 5.59 (ddd, *J* = 9.4, 4.5, 2.5 Hz, 1H), 5.48 (dd, *J* = 10.0, 8.1 Hz, 1H), 5.35 (d, *J* = 12.1 Hz, 1H), 5.26 (dd, *J* = 9.4, 2.7 Hz, 1H), 5.23 (m, 2H), 5.11 (t, *J* = 5.9 Hz, 1H), 5.03 (q, *J* = 12.4 Hz, 2H), 4.98 (d, *J* = 12.1 Hz, 1H), 4.90 (dd, *J* = 7.2, 2.7 Hz, 1H), 4.86 (m, 2H), 4.68 (m, 5H), 4.48 (d, *J* = 11.6 Hz, 1H), 4.40 (m, 2H), 4.32 (m, 1H), 4.28 (dd, *J* = 11.8, 4.5 Hz, 1H), 4.24 (d, *J* = 6.6 Hz, 1H), 4.14 (d, *J* = 11.3 Hz, 1H), 4.08 (dd, *J* = 12.7, 4.6 Hz, 1H), 3.99 (dd, *J* = 10.0, 3.8 Hz, 2H), 3.91 (t, *J* = 7.0 Hz, 2H), 3.83 (m, 3H), 3.72 (dd, *J* = 11.7, 6.9 Hz, 1H), 3.66 (m, 2H), 3.52 (dd, *J* = 11.8, 6.2 Hz, 1H), 3.43 (m, 3H), 3.22 (m, 1H), 3.14 (m, 1H), 3.05 (m, 1H), 2.74 (m, 2H), 2.60 (m, 2H), 2.43 (dd, *J* = 12.6, 4.5 Hz, 1H), 2.20 (s, 3H), 2.18 (s, 3H), 2.06 (s, 3H), 1.88 (s, 3H), 1.83 (s, 3H), 1.77 (s, 3H), 1.72 (t, *J* = 12.5 Hz, 1H), 1.61 (m, 1H), 1.58 (s, 3H), 1.55 (m, 1H), 1.25 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 206.94, 172.21, 170.82, 170.44, 170.19, 169.91, 167.63, 165.37, 156.55, 138.87, 138.81,

138.49, 134.41, 133.78, 133.44, 130.20, 130.08, 129.59, 129.26, 128.73, 128.67, 128.56, 128.46, 128.35, 128.26, 128.19, 128.10, 128.04, 127.98, 127.92, 127.65, 127.36, 127.32, 127.13, 100.58, 99.99, 96.99, 96.79, 79.13, 78.47, 76.21, 74.91, 74.18, 74.14, 73.73, 73.14, 72.76, 72.37, 72.18, 71.23, 71.06, 69.80, 69.08, 68.55, 67.64, 66.82, 66.44, 66.37, 62.92, 62.01, 60.75, 48.76, 37.82, 37.53, 37.24, 29.87, 29.35, 27.91, 23.31, 23.14, 21.54, 20.82, 20.66, 20.42, 16.72; ESI-MS: *m/z*: Calcd for $C_{97}H_{111}N_3NaO_{33}$ $[M+Na]^+$: 1868.7, found: 1869.0.

3-([(Benzyloxy)carbonyl]amino)propyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-(2,4-di-*O*-benzoyl-6-*O*-sulfo-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-6-*O*-levulinyl-β-D-glucopyranoside sodium salt (30). According to the procedure for **26**, compound **29** (116 mg, 62.8 µmol) was reacted with SO_3-pyridine (100 mg, 628 µmol) in DMF (1 mL) for 2 h to yield **30** (104 mg, 53.4 µmol, 85%) as an off-white glassy solid.

$[\alpha]_D^{20}$ -6.85 (*c* 1.00, DCM/MeOH, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 7.4 Hz, 2H), 7.98 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 3H), 7.49 (d, *J* = 7.3 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.23 (m, 23H), 6.76 (t, *J* = 7.1 Hz, 1H), 6.08 (d, *J* = 9.9 Hz, 1H), 5.62 (d, *J* = 8.5 Hz), 5.52 (t, *J* = 9.0 Hz, 1H), 5.37 (d, *J* = 12.0 Hz, 1H), 5.24 (d, *J* = 9.6 Hz, 1H), 5.19 (d, *J* = 2.9 Hz, 1H), 5.10 (d, *J* = 12.5 Hz, 1H), 5.05 (s, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.89 (m, 3H), 4.71 (m, 5H), 4.43 (m, 3H), 4.37 (d, *J* = 11.9 Hz, 1H), 4.30 (d, *J* = 11.8 Hz, 1H), 4.11 (m, 7H), 3.90 (m, 3H), 3.77 (m, 2H), 3.65 (d, *J* = 10.7 Hz, 1H), 3.59 (t, *J* = 10.0 Hz, 1H), 3.53 (d, *J* = 8.0 Hz, 1H), 3.47 (t, *J* = 10.9 Hz, 1H), 2.81 (m, 7H), 2.43 (dd, *J* = 12.3, 4.1 Hz, 1H), 2.24 (s, 3H), 2.22 (s, 3H), 2.07 (s, 3H), 1.88 (s, 6H), 1.74 (s, 3H), 1.70 (t, *J* = 12.5 Hz, 1H), 1.65 (m, 1H), 1.50 (d, *J* = 6.4 Hz, 3H), 1.47 (s, 3H), 1.41 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 208.49, 172.37, 172.24, 171.13, 170.64, 170.52, 170.01, 167.44, 166.58, 164.90, 157.07, 138.77, 138.04, 136.99, 136.61, 134.42, 133.57, 133.50, 130.24, 129.81, 129.40, 128.80, 128.65, 128.42, 128.20, 128.10, 128.04, 127.92, 127.72, 127.62, 127.55, 127.35, 127.21, 100.83, 100.18, 99.99, 97.85, 96.86, 79.08, 78.04, 75.03, 74.42, 74.04, 73.66, 72.99, 71.69, 71.55, 70.94, 70.87, 70.28, 69.36, 68.61, 67.31, 66.92, 66.84, 66.64, 66.32, 65.77, 62.07, 61.84, 54.62, 48.16, 37.99, 37.10, 36.12, 29.60, 29.54, 28.12, 22.69, 22.48, 21.43, 20.60, 20.52, 20.14, 16.78; ESI-MS: *m/z*: Calcd for $C_{97}H_{110}N_3Na_2O_{36}S$ $[M+Na]^+$: 1970.6, found: 1971.4.

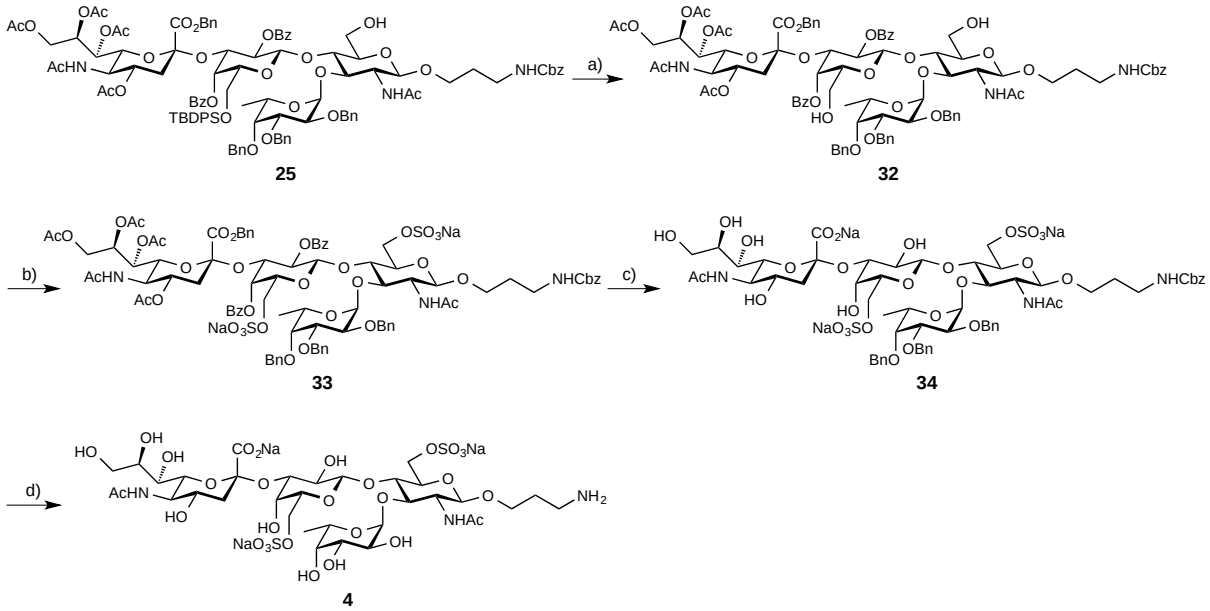
3-([(Benzyloxy)carbonyl]amino)propyl (5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-(6-*O*-sulfo-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-β-D-glucopyranoside disodium salt (31). According to the procedure for **28**, compound **30** (16 mg, 8.1 µmol) was treated with NaOMe/MeOH (0.5 mL) overnight to yield **31** (10 mg, 7.3 µmol, 90%) as an off-white glassy solid.

^{1}H NMR (500 MHz, D_2O): δ = 7.43 (m, 20H), 5.37 (s, 1H), 5.11 (s, 2H), 4.82 (s, 1H), 4.72 (m, 3H), 4.67 (d, *J* = 11.2 Hz, 1H), 4.57 (m, 2H), 4.45 (d, *J* = 7.4 Hz, 1H), 4.22 (m, 2H), 4.11 (m, 2H), 3.95 (m, 13H), 3.68 (m, 9H), 3.16 (m, 2H), 2.81 (dd, *J* = 12.3, 4.5 Hz, 1H), 2.06 (s, 3H), 1.97 (s, 3H), 1.83 (t, *J* = 12.1 Hz, 1H), 1.73 (m, 2H), 1.16 (d, *J* = 6.5 Hz, 3H); ESI-MS: *m/z*: Calcd for $C_{63}H_{81}N_3O_{28}S$ $[M-2Na]^{2-}$: 679.7, found: 679.8.

3-Aminopropyl 6′-sulfo sialyl Lewis^x disodium salt (3). According to the procedure for **2**, compound **31** (22 mg, 10.7 µmol) was hydrogenated with $Pd(OH)_2$/C (5 mg) in MeOH/H_2O (1:1, 0.3 mL) to yield **3** (8) (9 mg, 9.0 µmol, 49%) as an off-white glassy solid.

^{1}H NMR (500 MHz, D_2O): δ = 5.09 (d, *J* = 4.0 Hz, 1H), 4.78 (m, 1H), 4.52 (d, *J* = 7.9 Hz, 1H), 4.50 (d, *J* = 8.3 Hz, 1H), 4.13 (dd, *J* = 10.5, 4.6 Hz, 1H), 4.08 (m, 2H), 3.80 (m, 22H), 3.52 (dd, *J* = 9.8, 7.9 Hz, 1H), 3.06 (t, *J* = 6.9 Hz, 2H), 2.75 (dd, *J* = 12.4, 4.6 Hz, 1H), 2.01 (s, 6H), 1.92 (m, 2H), 1.77 (t, *J* = 12.1 Hz, 1H), 1.15 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, D_2O): δ = 175.04, 174.36, 173.74, 101.43, 101.02, 99.78, 98.48, 75.51, 75.25, 75.04, 73.66, 72.95, 72.35, 72.00, 71.83, 69.16, 69.12, 68.29, 68.13, 68.03, 67.86, 67.47, 67.10, 66.70, 62.64, 59.74, 55.75, 51.68, 39.76, 37.75, 26.72, 22.20, 22.03, 15.34; ESI-MS: *m/z*: Calcd for $C_{34}H_{57}N_3NaO_{26}S$ $[M-Na]^-$: 978.3, found: 978.3.

Synthesis of 6,6′-disulfo sialyl Lewis^x (4):



Scheme S7. a) HF-pyr, pyridine, rt, 30 min (88%); b) SO_3-pyr, DMF, 40 min (90%); c) NaOMe, MeOH, 8 h (92%); d) H_2, $Pd(OH)_2$/C, H_2O/MeOH, 16 h (69%).

3-([(Benzyloxy)carbonyl]amino)propyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-(2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-β-D-glucopyranoside (32). According to the procedure for **27**, compound **25** (22 mg, 11.1 µmol) was treated with HF-pyridine (0.17 mL) in pyridine (0.5 mL) for 30 min at rt to yield **32** (17 mg, 9.7 µmol, 88%) as a white glassy solid.

$[\alpha]_D^{20}$ -12.7 (*c* 1.00, DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 7.5 Hz, 2H), 8.03 (d, *J* = 7.2 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.52 (m, 3H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.30 (m, 14H), 7.22 (m, 11H), 5.93 (d, *J* = 8.2 Hz, 1H), 5.73 (t, *J* = 8.0 Hz, 1H), 5.48 (dd, *J* = 10.0, 8.2 Hz, 1H), 5.38 (m, 2H), 5.25 (d, *J* = 3.4 Hz, 1H), 5.17 (d, *J* = 3.1 Hz, 1H), 5.10 (dd, *J* = 9.3, 2.3 Hz, 1H), 5.04 (s, 2H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.94 (d, *J* = 8.1 Hz, 1H), 4.89 (d, *J* = 10.3 Hz, 1H), 4.80 (dd, *J* = 10.1, 3.3 Hz, 1H), 4.63 (m, 5H), 4.46 (m, 3H), 4.28 (d, *J* = 7.5 Hz, 1H), 4.08 (d, *J* = 11.3 Hz, 1H), 3.98 (m, 2H), 3.88 (m, 7H), 3.67 (m, 4H), 3.49 (dd, *J* = 12.0, 6.0 Hz, 1H), 3.36 (d, *J* = 1.9 Hz, 1H), 3.27 (s, 2H), 3.18 (s, 2H), 3.08 (m, 1H), 2.45 (dd, *J* = 12.6, 4.5 Hz, 1H), 2.25 (s, 3H), 2.06 (s, 3H), 1.88 (s, 6H), 1.78 (s, 3H), 1.76 (s, 3H), 1.69 (t, *J* = 12.5 Hz, 1H), 1.63 (m, 1H), 1.57 (m, 1H), 1.53 (s, 3H), 1.28 (d, *J* = 6.4 Hz, 3H); ESI-MS: *m/z*: Calcd for $C_{92}H_{105}N_3Na_2O_{31}$ $[M+2Na]^{2+}$: 896.8, found: 897.0.

3-([(Benzyloxy)carbonyl]amino)propyl (benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-(2,4-di-*O*-benzoyl-6-*O*-sulfo-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-6-*O*-sulfo-β-D-glucopyranoside disodium salt (33). According to the procedure for **26**, compound **32** (17 mg, 9.7 μmol) was reacted with SO_3-pyridine (26 mg, 163 μmol) in DMF (0.3 mL) for 40 min to yield **33** (17 mg, 8.7 μmol, 90%) as an off-white glassy solid.

$[\alpha]_D^{20}$ -21.4 (*c* 1.00, MeOH); ^{1}H NMR (500 MHz, CD_3OD): δ = 8.31 (d, *J* = 7.3 Hz, 2H), 8.04 (m, 2H), 7.67 (t, *J* = 7.3 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.38-7.12 (m, 23H), 5.53 (m, 3H), 5.31 (m, 2H), 5.22 (m, 2H), 5.05 (m, 4H), 4.79 (m, 4H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.51 (dd, *J* = 12.8, 2.5 Hz, 1H), 4.40 (m, 5H), 4.13 (m, 7H), 3.89 (m, 4H), 3.77 (m, 2H), 3.45 (m, 1H), 3.32 (m, 1H) 3.21 (m, 1H), 3.08 (m, 1H), 2.39 (dd, *J* = 12.6, 4.7 Hz, 1H), 2.12 (s, 3H), 2.05 (s, 3H), 1.96 (s, 3H), 1.89 (s, 3H), 1.86 (s, 3H), 1.78 (s, 3H), 1.79 (m, 1H), 1.65 (m, 2H), 1.37 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, CD_3OD): δ = 173.48, 173.35, 172.67, 171.94, 171.67, 171.57, 168.70, 168.08, 167.01, 158.88, 140.29, 140.25, 139.65, 138.62, 136.21, 134.71, 134.66, 131.64, 131.41, 131.14, 131.00, 130.15, 129.93, 129.60, 129.55, 129.50, 129.26, 129.24, 129.12, 129.11, 128.96, 128.77, 128.54, 128.39, 128.22, 102.61, 101.13, 99.15, 97.96, 80.22, 79.85, 76.35, 75.98, 75.31, 75.07, 73.98, 73.59, 73.25, 73.08, 72.71, 72.34, 70.75, 70.45, 69.20, 68.26, 67.98, 67.90, 67.36, 66.82, 63.13, 56.61, 50.03, 38.51, 37.99, 33.08, 30.78, 30.48, 23.74, 23.39, 22.65, 21.38, 21.04, 20.96, 20.63, 17.36; ESI-MS: *m/z*: Calcd for $C_{92}H_{103}N_3Na_3O_{37}S_2$ $[M+Na]^+$: 1974.5, found: 1975.1.

3-([(Benzyloxy)carbonyl]amino)propyl (5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosynate)-(2→3)-(6-*O*-sulfo-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-6-deoxy-α-L-galactopyranosyl)-(1→3)]-2-acetamido-2-deoxy-6-*O*-sulfo-β-D-glucopyranoside trisodium salt (34). According to the procedure for **28**, compound **33** (17 mg, 8.7 μmol) was treated with NaOMe/MeOH (0.5 mL) for 8 h to yield **34** (11 mg, 8.0 μmol, 92%) as an off-white glassy solid.

^{1}H NMR (500 MHz, D_2O): δ = 7.34 (m, 20H), 5.29 (d, *J* = 3.4 Hz, 1H), 5.05 (m, 2H), 4.73 (m, 1H), 4.62 (m, 5H), 4.49 (d, *J* = 11.6 Hz, 1H), 4.41 (d, *J* = 7.6 Hz, 1H), 4.30 (m, 2H), 4.15 (m, 2H), 4.04 (dd, *J* = 9.8, 3.2 Hz, 1H), 4.01 (d, *J* = 2.2 Hz, 1H), 3.85 (m, 11H), 3.71 (t, *J* = 6.7 Hz, 1H), 3.61 (m, 3H), 3.54 (dd, *J* = 9.1, 1.7 Hz, 1H), 3.50 (m, 1H), 3.46 (dd, *J* = 9.7, 7.9 Hz, 1H), 3.06 (m, 2H), 2.70 (dd, *J* = 12.4, 4.5 Hz, 1H), 1.97 (s, 3H), 1.90 (s, 3H), 1.76 (t, *J* =

12.1 Hz, 1H), 1.65 (m, 2H), 1.07 (d, *J* = 6.6 Hz, 3H); ESI-MS: *m/z*: Calcd for $C_{63}H_{81}N_3Na_3O_{31}S_2$ $[M+H]^+$: 1508.4, found: 1508.7.

3-Aminopropyl 6,6′-disulfo sialyl Lewis^x trisodium salt (4). According to the procedure for **2**, compound **34** (11 mg, 8.0 µmol) was hydrogenated with $Pd(OH)_2/C$ (5 mg) in $MeOH/H_2O$ (2:1, 2 mL) to yield **4** (6 mg, 5.5 µmol, 69%) as an off-white glassy solid.

$[\alpha]_D^{20}$ -31.3 (*c* 0.30, $MeOH/H_2O$, 5:1); ^1H NMR (500 MHz, D_2O): δ = 5.04 (d, *J* = 4.0 Hz, 1H), 4.73 (m, 3H), 4.54 (d, *J* = 7.9 Hz, 1H), 4.51 (d, *J* = 8.1 Hz, 1H), 4.34 (m, 2H), 3.83 (m, 17H), 3.54 (dd, *J* = 9.1, 1.6 Hz, 1H), 3.47 (dd, *J* =9.8, 7.9 Hz, 1H), 3.06 (t, *J* = 6.7 Hz, 2H), 2.69 (dd, *J* = 12.4, 4.6 Hz, 1H), 1.97 (s, 5H), 1.88 (m, 2H), 1.74 (t, *J* = 12.1 Hz, 1H), 1.11 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, D_2O): δ = 174.95, 174.35, 101.27, 100.98, 98.49, 75.21, 74.98, 73.27, 72.90, 72.21, 72.01, 71.39, 69.30, 69.10, 68.43, 68.30, 68.09, 67.86, 67.41, 67.05, 66.72, 66.11, 62.58, 55.50, 51.71, 39.65, 37.92, 26.65, 22.18, 22.04, 15.34; ESI-MS: *m/z*: Calcd for $C_{34}H_{56}N_3Na_2O_{29}S_2$ $[M-2Na+H]^-$: 1058.2, found: 1058.5.

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