Electronic supplementary information (Part1):

1,4-Dideoxy-1,4-imino-D- and L-lyxitol-based inhibitors bind to Golgi α-mannosidase II in different protonation forms

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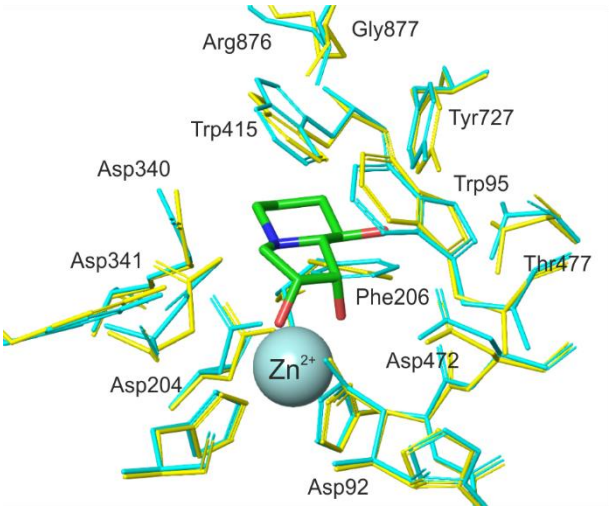

Figure S1. Superposition of dGMII (PDB ID: 3BLB, cyan) with a built homology model of AMAN-2 (yellow). The swainsonine bound to dGMII is visualized in green.

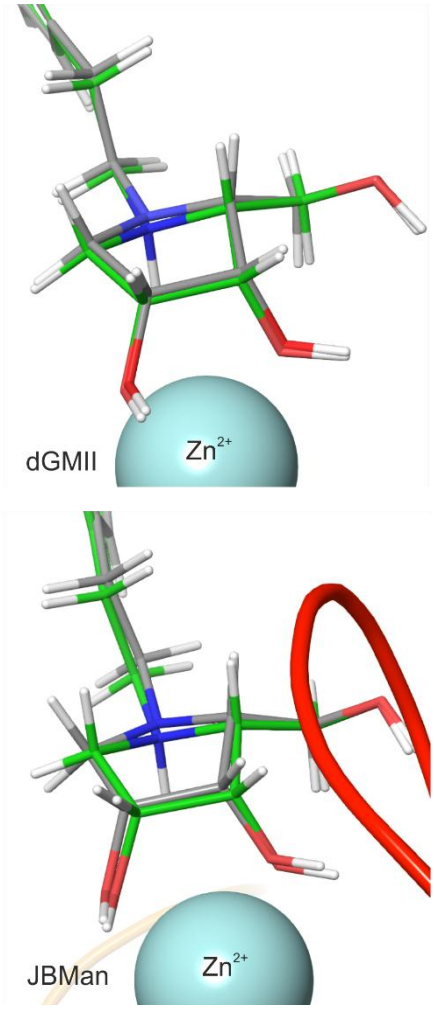

Figure S2. The compound **18** docked in neutral (gray) and protonated (green) forms into the active sites of dGMII and JBMan. The protonated forms are more tightly bound at the bottom of the active sites (where catalytic nucleophile Asp204 and Zn^{2+} ion reside) compared with the neutral forms.

Table S1. Predicted pK_a values for amino group of inhibitors and amino acid residues of dGMII in complexes enzyme-inhibitor using the Propka v.2 program (two forms of the complexes **enzyme-inhibitor^0** and **enzyme-inhibitor$^+$** were calculated. The structures of complexes were obtained from molecular docking).

PDB ID or name of structure	**inhibitor**	**Asp341**	**Asp340**	**Asp270**
3BUB(empty active site)-pdb		5.8	4.3	1.2
3BVX (substrate)-pdb		7.9	5.0	1.3
Swainsonine-1HWW-pdb Swainsonine-3BLB-pdb	5.3 5.0	5.6 5.6	3.1 4.3	6.4 1.1
2F1A-pdb	5.7 9.7 (linker)	0.6	4.1	6.4
2F1B-pdb	4.6 -3.0	5.8	2.4	6.4
2F18-pdb	5.6 9.5 (linker)	2.1	1.8	6.5
2FYV-pdb	4.9	5.9	1.5	6.1
DIM^0 DIM$^+$	4.9 5.4	5.9 5.7	0.9 0.9	4.4 4.1
6^0 **6**$^+$	4.9 5.0	5.7 5.5	0.9 1.1	4.4 4.2
4^0 **4**$^+$	7.8 5.3	3.6 5.8	0.3 1.1	4.0 4.4
6^0 **6**$^+$	5.5 5.4	5.9 5.8	-0.1 1.0	3.9 4.3
17^0 **17**$^+$	7.7 5.1	3.9 5.7	0.1 0.5	4.0 4.1
18^0 **18**$^+$	5.5 5.0	6.0 5.2	0.1 2.9	4.6 6.3
20^0 **20**$^+$	7.5 5.2	3.5 5.7	0.3 0.5	4.0 4.0
19^0 **19**$^+$	7.4 5.1	3.5 5.7	0.4 1.0	4.0 4.2
21^0 **21**$^+$	5.5 5.2	5.5 5.9	0.2 1.1	4.0 4.2
26^0 **26**$^+$	5.5 5.2	5.5 5.9	0.2 1.1	4.0 4.2
9$^+$	7.6 (N-pyrrolidine) 17.4 (N-guanidine)	2.9	-2.0	2.6

Table S2. Predicted pK_a values for amino group of inhibitors and amino acid residues of JBMan in complexes enzyme-inhibitor using the Propka v.2 program (two forms of the complexes **enzyme-inhibitor^0** and **enzyme-inhibitor$^+$** were calculated. The structures of complexes were obtained from molecular docking).

PDB ID or name of structure	**inhibitor**	**Asp268**	**Asp267**	**His209**
6b9o (empty active site)-pdb		7.4	-0.4	7.6
6b9p (ligand)-pdb	9.0	4.0	1.4	7.7
Swainsonine^0	8.1	2.7	0.1	8.9
Swainsonine$^+$	7.8	5.1	-0.3	7.9
DIM^0	7.7	3.2	1.2	7.8
DIM$^+$	7.4	3.2	1.2	7.8
6^0	7.3	3.3	1.2	7.8
6$^+$	7.3	3.2	1.2	7.8
4^0	7.8	3.4	1.3	7.8
4$^+$	8.5	3.3	1.3	7.6
16^0	7.9	3.3	1.3	7.8
16$^+$	8.2	3.3	1.4	7.6
17^0	7.4	4.9	1.5	7.6
17$^+$	7.4	4.6	1.5	7.6
18^0	8.0	3.7	1.5	7.6
18$^+$	8.0	4.1	1.5	7.7
19^0	8.0	3.4	1.3	7.8
19$^+$	8.1	3.3	1.3	7.8
20^0	7.9	3.4	1.3	7.8
20$^+$	8.0	3.4	1.3	7.7
21^0	8.0	3.4	1.3	7.8
21$^+$	8.1	3.3	1.3	7.8
25^0	8.1 (N-pyrridine) 13.4 (N-guanidine)	2.8	-1.6	5.7
25$^+$	8.1 (N-pyrridine) 9.4 (N-guanidine)	2.9	0.9	6.8
26^0	8.5 (N-pyrridine) 13.4 (N-amidine)	3.0	-1.4	6.6
26$^+$	8.4 (N-pyrridine) 12.2 (N-amidine)	3.1	-0.1	5.9

Experimental

General

TLC was performed on aluminum sheets pre-coated with silica gel 60 F254 (Merck). Visualization was achieved by immersing the plates into a 10% solution of phosphomolybdic acid (PMA) in ethanol followed by heating the plate. Flash column chromatography was carried out on silica gel 60 (0.040–0.060 mm, Merck) with distilled solvents. All commercially available reagents and anhydrous solvents were used as received. *p*-Nitrophenyl α-d-mannopyranoside (*p*NP-Man*p*) and jack bean α-mannosidase were purchased from Sigma; swainsonine and DIM from Biosynth. All reactions containing sensitive reagents were carried out under a nitrogen atmosphere. Melting point was determined using a Boetius PHMK 05 microscope. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C with the Bruker AVANCE III HD 400 spectrometer. Chemical shifts are given in ppm (δ) relative to the residual signal of appropriate deuterated solvent used. The ultrasonic bath USC-300TH was used for sonication. Optical rotations were determined on a Jasco P-2000 polarimeter at 20 °C. High-resolution mass spectra were recorded with an Orbitrap Elite (Thermo Scientific) mass spectrometer with ESI ionization in positive mode. The compounds for biological assays were lyophilized before the use.

Synthesis

General procedure for preparation of protected guanidines (Method A)

Amine (0.15 mmol, 1 eq) was dissolved in mixture of THF/DMF (4.5 mL, 2:1, v/v) and *N*,*N*′-bis(*tert*-butoxycarbonyl)-1*H*-pyrazole-1-carboxamidine (1.1 eq) was added. The mixture was sonicated at 45 °C for 1 h. The solvent was evaporated, the residue was diluted with water (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography (hexane/EtOAc).

General method for *N*-alkylation (Method B)

The protected d-lyxitol **5** (0.4 mmol, 1eq) was dissolved in DMF (3 mL), K_2CO_3 (2 eq) and corresponding bromide were added. The reaction mixture was stirred under conditions as indicated. Then, the mixture was poured into EtOAc/H_2O (30 mL, 1:1) at rt. The organic phase was separated, washed with water (2 x 20 mL). The organic extract was dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (hexane/EtOAc).

5-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-isopropylidene-L-ribitol (1)

Compound **1**[1] was prepared from L-ribose (7.07 g). Diol **1**[2,3] (6.64 g, 46% over 3 steps), white solid, mp 82-83.5 °C, $[\alpha]_D$ = - 32.7 (*c* 0.31, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.36 (dd, 1H, *J* 5.0 Hz, *J* 7.8 Hz, H-4), 4.06 (dd, 1H, *J* 6.0 Hz, *J* 9.6 Hz, H-3), 3.91-3.83 (m, 2H, H-1′, H-5), 3.82-3.76 (m, 2H, H-1, H-2), 3.66 (dd, 1H, *J* 6.0 Hz, *J* 9.9 Hz, H-5′), 3.16 (br s, 1H, OH-1), 3.04 (br s, 1H, OH-4), 1.40 and 1.34 (each s, each 3H, $C(CH_3)_2$), 0.91 (br s, 9H, $C(CH_3)_3$), 0.10 (s, 6H, $Si(CH_3)_2$).^{13}C NMR (100 MHz, $CDCl_3$): δ 108.7 ($C(CH_3)_2$), 77.7 (C-4), 76.7 (C-3), 69.6 (C-2), 64.5 (C-5), 61.0 (C-1), 28.0 ($C(CH_3)_2$), 26.0 ($C(CH_3)_3$), 25.4 ($C(CH_3)_2$), 18.5 ($C(CH_3)_3$), -5.2 and -5.3 ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{14}H_{28}O_5Si]H^+$: 305.1779, found: 305.1790.

5-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-isopropylidene-1,4-di-*O*-methanesulfonyl-L-ribitol (2)

Mesylation of **1** (6.50 g, 21.2 mmol) carried out following the reported procedure [1] afforded dimesylate **2** (8.73 g, 89%), colorless oil, $[\alpha]_D$ = - 9.7 (*c* 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.81 (ddd, 1H, *J* 2.8 Hz, *J* 4.2 Hz, *J* 7.1 Hz, H-4), 4.52 (dd, 1H, *J* 3.3 Hz, *J* 10.6 Hz, H-1′), 4.49-4.44 (m, 1H, H-2), 4.38-4.33 (m, 2H, H-1, H-3), 4.07 (dd, 1H, *J* 2.8 Hz, *J* 12.1 Hz, H-5), 3.89 (dd, 1H, *J* 4.2 Hz, *J* 12.1 Hz, H-5′), 3.13 and 3.07 (each s, each 3H, 2 × SO_2CH_3), 1.49 and 1.37 (each s, each 3H, 2 × $C(CH_3)_2$), 0.91 (br s, 9H, $C(CH_3)_3$), 0.10 (2x) (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.6 ($C(CH_3)_2$), 79.8 (C-4), 75.2 (C-2), 74.2 (C-3), 68.7 (C-1), 62.8 (C-5), 39.4, 37.7 (2 × SO_2CH_3), 27.7 ($C(CH_3)_2$), 26.0 ($C(CH_3)_3$), 25.6 ($C(CH_3)_2$), 18.5 ($C(CH_3)_3$), -5.3 and -5.4 ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{16}H_{34}O_9S_2Si]Na^+$: 485.1306, found: 485.1310.

N-Benzyl-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (3)

The reaction of dimesylate **2** (8.0 g, 17.3 mmol) and benzylamine (60 mL) carried out following the reported procedure [1] afforded compound **3** (5.74 g, 88%), yellow oil, $[\alpha]_D$ = - 83.6 (*c* 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.18 (m, 5H, Ar), 4.64 (dd, 1H, *J* 4.6 Hz, *J* 6.5 Hz, H-3), 4.55 (dd, 1H, *J* 4.6 Hz, *J* 6.4 Hz, H-2), 4.25 (d, 1H, *J* 13.7 Hz, NCH_2), 4.01 (dd, 1H, *J* 5.6 Hz, *J* 10.4 Hz, H-5), 3.84 (dd, 1H, *J* 5.6 Hz, *J* 10.4 Hz, H-5′), 3.20 (d, 1H, *J* 13.7 Hz, NCH_2), 3.01 (d, 1H, *J* 11.2 Hz, H-1′), 2.39 (q, 1H, *J* 5.4 Hz, H-4), 2.00 (dd, 1H, *J* 4.7 Hz, *J* 11.2 Hz, H-1), 1.52 and 1.30 (each s, each 3H, 2 × $C(CH_3)_2$), 0.90 (br s, 9H, $C(CH_3)_3$), 0.08 and 0.07 (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 128.7, 128.3, 126.8 (Ar), 111.2 ($C(CH_3)_2$), 81.1 (C-3), 78.1 (C-2), 69.6 (C-4), 62.5 (C-5), 60.1 (C-1), 58.2 (NCH_2), 26.5 ($C(CH_3)_2$), 26.1 ($C(CH_3)_3$), 25.8 ($C(CH_3)_2$),

18.5 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{21}H_{35}NO_3Si]H^+$: 378.2459, found: 378.2450.

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (5)

To the solution of **3** (5.7 g, 15.1 mmol) in MeOH (300 mL), 10% Pd/C was added. The solution was stirred under a hydrogen atmosphere for 6 h. The catalyst was then filtered off through pad of Celite and the solvent was evaporated. The crude product was purified by column chromatography (hexane/EtOAc/NH_3 4:1:0→1:6:0.1, v/v/v). Amine **5** (3.52 g, 81%), yellowish oil, $[\alpha]_D$ = - 65.1 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.66 (dd, 1H, *J* 4.5 Hz, *J* 6.5 Hz, H-2), 4.58 (dd, 1H, *J* 4.4 Hz, *J* 6.5 Hz, H-3), 3.86 (dd, 1H, *J* 6.6 Hz, *J* 10.1 Hz, H-5′), 3.77 (dd, 1H, *J* 6.2 Hz, *J* 10.1 Hz, H-5), 3.09 (d, 1H, *J* 12.9 Hz, H-1′), 2.80 (q, 1H, *J* 6.3 Hz, H-4), 2.65 (dd, 1H, *J* 4.0 Hz, *J* 12.9 Hz, H-1), 1.72 (s, 1H, NH), 1.44 and 1.30 (each s, each 3H, 2 × $C(CH_3)_2$), 0.89 (br s, 9H, $C(CH_3)_3$), 0.07 (br s, 6H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 110.7 ($C(CH_3)_2$), 81.6 (C-2), 80.9 (C-3), 65.5 (C-4), 61.7 (C-5), 53.2 (C-1), 26.1 ($C(CH_3)_3$), 26.0 ($C(CH_3)_2$), 24.1 ($C(CH_3)_2$), 18.6 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{14}H_{29}NO_3Si]H^+$: 288.1989, found: 288.1987.

***N*-(4-Aminomethylbenzyl)-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (7)**

Dimesylate **2** (0.28 g, 0.6 mmol) and *p*-xylylenediamine (0.41 g, 3.02 mmol) were heated at 95 °C for 16 h. The reaction mixture was cooled to rt, diluted with EtOAc (30 mL) and washed with water (3 × 10 mL), the organic layer was separated, dried (Na_2SO_4), filtered and the solvent was evaporated. Purification of the crude product by column chromatography (hexane/EtOAc/Et_3N 4:1:0→1:5:0.1 v/v/v) afforded compound **7** (0.12 g, 50%), yellow oil, $[\alpha]_D$ = - 54.0 (*c* 0.29, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.22 (m, 4H, Ar), 4.64 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-3), 4.54 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-2), 4.23 (d, 1H, *J* 13.7 Hz, NCH_2), 4.01 (dd, 1H, *J* 5.6 Hz, *J* 10.4 Hz, H-5), 3.86-3.82 (m, 3H, H-5′, CH_2NH_2), 3.21 (d, 1H, *J* 13.7 Hz, NCH_2), 2.99 (d, 1H, *J* 11.1 Hz, H-1′), 2.39 (q, 1H, *J* 5.4 Hz, H-4), 2.00 (dd, 1H, *J* 4.7 Hz, *J* 11.2 Hz, H-1), 1.91 (br s, 2H, CH_2NH_2), 1.51 and 1.30 (each s, each 3H, 2 × $C(CH_3)_2$), 0.89 (br s, 9H, $C(CH_3)_3$), 0.08 and 0.07 (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 137.8, 129.0, 127.1 (Ar), 111.3 ($C(CH_3)_2$), 81.1 (C-3), 78.1 (C-2), 69.4 (C-4), 62.5 (C-5), 60.0 (C-1), 57.8 (NCH_2), 46.2 (CH_2NH_2), 26.5 ($C(CH_3)_2$), 26.1 ($C(CH_3)_3$), 25.8 ($C(CH_3)_2$), 18.5 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{22}H_{38}N_2O_3Si]H^+$: 407.2730, found: 407.2725.

***N*-(Benzyl-4-(2,3-bis(*tert*-butyloxycarbonyl)guanidino)methyl)-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (8)**

Guanidine derivative **8** was prepared from **7** (0.12 g, 0.29 mmol) following general procedure Method A. Purification of the crude product by column chromatography (hexane/EtOAc 10:1→4:1) afforded **8** (0.12 g, 64%), yellow oil, $[\alpha]_D$ = - 34.0 (*c* 0.22, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.22 (m, 4H, Ar), 4.64 (dd, 1H, *J* 4.8 Hz, *J* 6.4 Hz, H-3), 4.59 (d, 2H, *J* 5.0 Hz, ArCH_2guan), 4.55 (dd, 1H, *J* 4.6 Hz, *J* 6.4 Hz, H-2), 4.24 (d, 1H, *J* 13.8 Hz, NCH_2), 4.00 (dd, 1H, *J* 5.5 Hz, *J* 10.4 Hz, H-5), 3.83 (dd, 1H, *J* 5.7 Hz, *J* 10.4 Hz, H-5′), 3.20 (d, 1H, *J* 13.8 Hz, NCH_2), 3.01 (d, 1H, *J* 11.1 Hz, H-1′), 2.39 (q, 1H, *J* 5.4 Hz, H-4), 1.99 (dd, 1H, *J* 4.7 Hz, *J* 11.2 Hz, H-1), 1.52 (s, 12H, $C(CH_3)_2$, Boc), 1.48 (s, 9H, Boc), 1.30 (s, 3H, $C(CH_3)_2$), 0.89 (br s, 9H, $C(CH_3)_3$), 0.08 and 0.06 (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8 (C, guan), 156.2 (C=O), 153.3 (C=O), 138.8, 135.7, 129.0, 127.9 (Ar), 111.3 ($C(CH_3)_2$), 83.1 (^{t}Bu, Boc), 81.0 (C-3), 79.5 (^{t}Bu, Boc), 78.1 (C-2), 69.6 (C-4), 62.6 (C-5), 60.0 (C-1), 57.9 (NCH_2), 45.0 (ArCH_2guan), 28.5 (Boc), 28.2 (Boc) 26.5 ($C(CH_3)_2$), 26.1 ($C(CH_3)_3$), 25.8 ($C(CH_3)_2$), 18.4 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{33}H_{56}N_4O_7Si]H^+$: 649.3991, found: 649.4005.

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-*N*-4-iodobenzyl-2,3-*O*-isopropylidene-D-lyxitol (10)

The reaction of **5** (0.25 g, 0.87 mmol) and 4-iodobenzylbromide (0.28 g, 0.96 mmol, 1.1eq) was carried out at 45 °C for 4 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1→10:1) afforded compound **10** (0.40 g, 90%), yellowish oil, $[\alpha]_D$ = - 64.3 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, 2H, *J* 8.2 Hz, Ar), 7.08 (d, 2H, *J* 8.2 Hz, Ar), 4.63 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-3), 4.55 (dd, 1H, *J* 4.6 Hz, *J* 6.4 Hz, H-2), 4.21 (d, 1H, *J* 14.0 Hz, NCH_2), 4.00 (dd, 1H, *J* 5.2 Hz, *J* 10.5 Hz, H-5′), 3.81 (dd, 1H, *J* 5.9 Hz, *J* 10.5 Hz, H-5), 3.15 (d, 1H, *J* 14.0 Hz, NCH_2), 2.98 (d, 1H, *J* 11.1 Hz, H-1′), 2.39 (q, 1H, *J* 5.2 Hz, H-4), 1.98 (dd, 1H, *J* 4.6 Hz, *J* 11.1 Hz, H-1), 1.50 and 1.30 (each s, each 3H, 2 × $C(CH_3)_2$), 0.89 (br s, 9H, $C(CH_3)_3$), 0.07 and 0.06 (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 137.4, 130.6 (Ar), 111.3 ($C(CH_3)_2$), 92.1 (Ar), 81.0 (C-3), 78.1 (C-2), 69.4 (C-4), 62.8 (C-5), 60.1 (C-1), 57.8 (NCH_2), 26.5 ($C(CH_3)_2$), 26.1 ($C(CH_3)_3$), 25.7 ($C(CH_3)_2$), 18.54 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{21}H_{34}NO_3SiI]H^+$: 504.1425, found: 504.1430.

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*N*-(naphthalen-2-ylmethyl)-D-lyxitol (11)

The reaction of **5** (0.12 g, 0.42 mmol) and 2-(bromomethyl)naphthalene (0.10 g, 0.46 mmol, 1.1eq) was carried out at 45 °C for 4 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1→10:1) afforded compound **11** (0.15 g, 84%), yellow oil, $[\alpha]_D$ = - 26.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.75 (m, 4H, Ar), 7.52-7.42 (m, 3H, Ar), 4.66 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-3), 4.56 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-2), 4.42 (dd, *J* 1.1 Hz, *J* 13.8 Hz, NCH_2), 4.06 (dd, 1H, *J* 5.5 Hz, *J* 10.5 Hz, H-5′), 3.91 (dd, 1H, *J* 5.8 Hz, *J* 10.4 Hz, H-5), 3.38 (d, 1H, *J* 13.8 Hz, NCH_2), 3.03 (d, 1H, *J* 11.2 Hz, H-1′), 2.47 (q, 1H, *J* 5.3 Hz, H-4), 2.06 (dd, 1H, *J* 4.7 Hz, *J* 11.2 Hz, H-1), 1.56 and 1.31 (each s, each 3H, 2 × $C(CH_3)_2$), 0.91 (br s, 9H, $C(CH_3)_3$), 0.10 and 0.08 (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 133.5, 132.8, 127.9, 127.8, 127.8, 127.3, 127.0, 126.0, 125.5 (Ar), 111.3 ($C(CH_3)_2$), 81.1 (C-3), 78.2 (C-2), 69.6 (C-4), 62.6 (C-5), 60.2 (C-1), 58.4 (NCH_2), 26.6 ($C(CH_3)_2$), 26.1 ($C(CH_3)_3$), 25.8 ($C(CH_3)_2$), 18.5 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{25}H_{37}NO_3Si]H^+$: 428.2615, found: 428.2616.

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*N*-(2-(naphthalen-1-yl)ethyl)-D-lyxitol (12)

The reaction of **5** (0.10 g, 0.35 mmol) and 1-(2-bromoethyl)naphthalene (90 mg, 54.7 µL, 0.38 mmol, 1.1eq) was carried out at 45 °C for 24 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1→10:1) afforded compound **12** (0.10 g, 66%), yellow oil, $[\alpha]_D$ = - 40.3 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, 1H, *J* 8.3 Hz, Ar), 7.86-7.83 (d, 1H, Ar), 7.70 (dd, 1H, *J* 1.7 Hz, *J* 7.5 Hz, Ar), 7.53-7.44 (m, 2H, Ar), 7.40-7.35 (m, 2H, Ar), 4.67-4.62 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.3 Hz, *J* 10.2 Hz, H-5′), 3.71 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H-5), 3.46 (d, 1H, *J* 10.8 Hz, H-1′), 3.47-3.20 (m, 3H, NCH_2, NCH_2CH_2), 2.46 (ddd, 1H, *J* 4.9 Hz, *J* 9.2 Hz, *J* 10.1 Hz, NCH_2CH_2), 2.33 (q, 1H, *J* 5.6 Hz, H-4), 2.26 (dd, 1H, *J* 4.3 Hz, *J* 10.8 Hz, H-1), 1.51 and 1.33 (each s, each 3H, 2 × $C(CH_3)_2$), 0.82 (br s, 9H, $C(CH_3)_3$), 0.02 and 0.01 (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 134.0, 132.1, 128.9, 126.8, 126.6, 126.0, 125.6, 125.5, 123.9 (Ar), 111.1 ($C(CH_3)_2$), 80.8 (C-3), 78.2 (C-2), 70.1 (C-4), 62.0 (C-5), 60.4 (C-1), 55.4 (NCH_2), 31.7 (NCH_2CH_2), 26.4 ($C(CH_3)_2$), 26.0 ($C(CH_3)_3$), 25.5 ($C(CH_3)_2$), 18.4 ($C(CH_3)_3$), -5.3(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{26}H_{39}NO_3Si]H^+$: 442.2772, found: 442.2779.

5-*O*-*tert*-Butyldimethylsilyl-*N*-cyclohexylmethyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (13)

The reaction of **5** (0.12 g, 0.42 mmol) and cyclohexyl bromide (0.11 g, 90.3 µL, 0.65 mmol, 1.5 eq) was carried out at 60 °C for 16 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1→10:1) afforded compound **13** (87.2 mg, 53%), yellow oil, $[\alpha]_D$ = - 38.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.62-4.57 (m, 2H, H-2, H-3), 3.90 (dd, 1H, *J* 6.1 Hz, *J* 10.2 Hz, H-5′), 3.69 (dd, 1H, *J* 5.3 Hz, *J* 10.2 Hz, H-5), 3.18 (d, 1H, *J* 10.9 Hz, H-1′), 2.64 (dd, 1H, *J* 10.6 Hz, *J* 12.0 Hz, NCH_2), 2.16 (q, 1H, *J* 5.4 Hz, H-4) 1.98-1.86 (m, 2H, NCH_2, Cyh), 1.92 (dd, 1H, *J* 4.3 Hz, *J* 11.0 Hz, H-1), 1.69-1.57 (m, 5H, Cyh), 1.47 and 1.30 (each s, each 3H, $C(CH_3)_2$), 1.22-1.12 (m, 3H, Cyh), 0.90 (br s, 9H, $C(CH_3)_3$), 0.87-0.74 (m, 2H, Cyh), 0.07(2x) (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 111.2 ($C(CH_3)_2$), 81.0 (C-3), 78.5 (C-2), 70.6 (C-4), 62.2 (C-5), 61.5 (NCH_2), 60.8 (C-1), 36.8 (CH), 32.3, 31.6, 27.1, 26.5, 26.4 (5 × CH_2), 26.2 ($C(CH_3)_2$), 26.1(4x) ($C(CH_3)_3$, ($C(CH_3)_2$), 18.4 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{21}H_{41}NO_3Si]H^+$: 384.2928, found: 384.2931.

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*N*-(tetrahydro-2*H*-pyran-4-yl)methyl)-D-lyxitol (14)

The reaction of **5** (0.13 g, 0.45 mmol) and 4-(bromomethyl)tetrahydro-pyran (0.12 g, 89.3 µL, 0.68 mmol, 1.5 eq) was carried out at 60 °C for 16 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1→7:1) afforded compound **14** (84 mg, 49%), yellow oil, $[\alpha]_D$ = - 54.0 (*c* 0.28, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.62-4.58 (m, 2H, H-2, H-3), 3.97-3.89 (m, 3H, NCH_2, H-5′), 3.69 (dd, 1H, *J* 5.6 Hz, *J* 10.4 Hz, H-5), 3.36 (dq, 2H, *J* 2.2 Hz, *J* 12.0 Hz, THP), 3.18 (d, 1H, *J* 10.9 Hz, H-1′), 2.76 (dd, 1H, *J* 10.6 Hz, *J* 12.1 Hz, THP), 2.21 (q, 1H, *J* 5.2 Hz, H-4), 1.99-1.93 (m, 2H, H-1, THP), 1.86 (ddd, 1H, *J* 2.1 Hz, *J* 4.0 Hz, *J* 13.6 Hz, THP), 1.61-1.48 (m, 2H, THP), 1.45 and 1.30 (each s, each 3H, $C(CH_3)_2$), 1.23-1.17 (m, 2H, THP), 0.90 (br s, 9H, $C(CH_3)_3$), 0.07(2x) (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 111.2 ($C(CH_3)_2$), 81.0 (C-3), 78.4 (C-2), 70.4 (C-4), 68.3 (NCH_2), 68.0 (CH_2), 62.4 (C-5), 60.8, 60.7 (C-1, CH_2), 34.3 (CH), 32.0, 31.8 (2 × CH_2), 26.5 ($C(CH_3)_2$), 26.1(3x) ($C(CH_3)_3$), 25.9 ($C(CH_3)_2$), 18.4 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{20}H_{39}NO_4Si]H^+$: 386.2721, found: 386.2722.

5-*O*-*tert*-Butyldimethylsilyl-1,4-dideoxy-*N*-dodecyl-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (15)

The reaction of **5** (0.14 g, 0.49 mmol) and 1-bromododecane (0.13 g, 0.13 mL, 0.53 mmol, 1.1eq) was carried out at 45 °C for 4 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1→6:1) afforded compound **15** (0.15 g, 68%), yellow oil, $[\alpha]_D$ = - 34.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63-4.57 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.3 Hz, *J* 10.2 Hz, H-5′), 3.75 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H-5), 3.21 (d, 1H, *J* 11.0 Hz, H-1′), 2.90 (dt, 1H, *J* 7.7 Hz, *J* 11.9 Hz, NCH_2), 2.22 (q, 1H, *J* 5.3 Hz, H-4), 2.04-1.97 (m, 2H, H-1, NCH_2), 1.48-1.42 (m, 5H, CH_2, $C(CH_3)_2$), 1.30 (s, 3H, $C(CH_3)_2$), 1.28-1.22 (m, 18H, 9 × CH_2), 0.92-0.86 (m, 12H, CH_3, $C(CH_3)_3$), 0.07(2x) (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 111.0 ($C(CH_3)_2$), 80.9 (C-3), 78.1 (C-2), 70.3 (C-4), 62.0 (C-5), 60.1 (C-1), 54.6 (NCH_2), 32.1, 29.8(2x), 29.7, 29.5, 28.0, 27.7, 26.1(2x), 22.8 (10 × CH_2), 26.3 ($C(CH_3)_2$), 26.1 ($C(CH_3)_3$), 25.6 ($C(CH_3)_2$), 18.4 ($C(CH_3)_3$), 14.3 (CH_3), -5.2(2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z*: calcd for $[C_{26}H_{53}NO_3Si]H^+$: 456.3868, found: 456.3874.

5-*O*-*tert*-Butyldimethylsilyl-*N*-(9-cyanononyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (22)
The reaction of **5** (0.60 g, 2.08 mmol) and 10- bromodecanenitrile [4] (0.54 g, 2.30 mmol, 1.1 eq) was carried out at 45 °C for 16 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1→6:1) afforded compound **22** (0.8 g, 87%), yellow oil, $[\alpha]_D$ = - 74.7 (*c* 0.21, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.62-4.55 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.2 Hz, *J* 10.2 Hz, H-5′), 3.74 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H- 5), 3.20 (d, 1H, *J* 11.0 Hz, H-1′), 2.91 (ddd, 1H, *J* 7.4 Hz, *J* 8.8 Hz, *J* 12.0 Hz, NCH_2), 2.33 (t, 2H, *J* 7.1 Hz, CH_2CN), 2.22 (q, 1H, *J* 5.6 Hz, H-4), 2.04-1.97 (m, 2H, H- 1, NCH_2), 1.68-1.61 (m, 2H, CH_2), 1.47 (s, 3H, $C(CH_3)_2$), 1.46-1.40 (m, 4H, 2 × CH_2), 1.32-1.27 (m, 8H, 4 × CH_2), 1.30 (s, 3H, $C(CH_3)_2$), 0.90 (br s, 9H, $C(CH_3)_3$), 0.07(2x) (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 120.0 (CN), 111.0 ($C(CH_3)_2$), 80.9 (C-3), 78.1 (C-2), 70.4 (C- 4), 62.1 (C-5), 60.1 (C-1), 54.6 (NCH_2), 29.5, 29.4, 28.9, 28.8, 28.0, 27.6 (6 × CH_2), 26.4 ($C(CH_3)_2$), 26.1(3x) ($C(CH_3)_3$), 25.5(2x) (CH_2, $C(CH_3)_2$), 18.4 ($C(CH_3)_3$), 17.3 (CH_2), -5.2(2x) ($Si(CH_3)_2$). HRMS: *m/z* calcd for $[C_{24}H_{46}N_2O_3Si]H^+$: 439.3350, found: 439.3347.

***N*-(10-Aminodecyl)-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (23)**
Lithium triethylborohydride (0.32 g, 1.82 mL, 1.7M in THF) was added dropwise to a solution of nitrile **22** (0.14 g, 0.31 mmol) in THF (8 mL) at 0 °C. The solution was sonicated at 50 °C for 2 h. The mixture was slowly poured into cold water (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. Purification of the crude product by column chromatography ($CHCl_3$/MeOH/NH_3 1:0:0→10:1:0→7:1:0.1, v/v/v) afforded compound **23** (0.13 g, 89%), yellow oil, $[\alpha]_D$ = - 31.2 (*c* 0.31, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.62-4.55 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.2 Hz, *J* 10.1 Hz, H-5′), 3.74 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H- 5), 3.20 (d, 1H, *J* 11.0 Hz, H-1′), 2.89 (dt, 1H, *J* 7.7 Hz, *J* 12.0 Hz, NCH_2), 2.71 (t, 2H, *J* 7.2 Hz, CH_2NH_2), 2.21 (q, 1H, *J* 5.6 Hz, H-4), 2.02-1.96 (m, 2H, H-1, NCH_2), 1.47 (s, 3H, $C(CH_3)_2$), 1.46-1.38 (m, 4H, 2 × CH_2), 1.32-1.27 (m, 12H, 6 × CH_2), 1.30 (s, 3H, $C(CH_3)_2$), 0.90 (br s, 9H, $C(CH_3)_3$), 0.07(2x) (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 111.0 ($C(CH_3)_2$), 80.8 (C-3), 78.1 (C-2), 70.4 (C-4), 62.0 (C-5), 60.1 (C-1), 54.7 (NCH_2), 41.3 (CH_2NH_2), 29.7(2x), 29.6(2x), 29.5, 28.0, 27.7, 26.9 (8 × CH_2), 26.3 ($C(CH_3)_2$), 26.1 (3x) ($C(CH_3)_3$), 25.5 ($C(CH_3)_2$), 18.4 ($C(CH_3)_3$), -5.2(2x) ($Si(CH_3)_2$). HRMS: *m/z* calcd for $[C_{24}H_{50}N_2O_3Si]H^+$: 443.3663, found: 443.3669.

5-*O*-*tert*-Butyldimethylsilyl-*N*-(10-(2,3-bis(*tert*-butyloxycarbonyl)guanidino)decyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (24)
Guanidine derivative **24** was prepared from amine **23** (57 mg, 0.13 mmol) following general procedure Method A. Purification of the crude product by column chromatography (hexane/EtOAc 40:1→10:1) afforded **24** (50 mg, 56%), yellowish oil, $[\alpha]_D$ = - 39.2 (*c* 0.27, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$): δ 4.63-4.56 (m, 2H, H-3, H-2), 3.92 (dd, 1H, *J* 6.3 Hz, *J* 10.2 Hz, H- 5′), 3.75 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H-5), 3.40 (td, 2H, *J* 5.4 Hz, *J* 7.3 Hz, CH_2NH), 3.21 (d, 1H, *J* 11.1 Hz, H-1′), 2.90 (dt, 1H, *J* 7.8 Hz, *J* 11.8 Hz, NCH_2), 2.22 (q, 1H, *J* 5.4 Hz, H- 4), 2.03-1.97 (m, 1H, 2H, H-1, NCH_2), 1.65-1.59 (m, 10H, 5 × CH_2), 1.50 (s, 9H, Boc), 1.49 (s, 9H, Boc), 1.47 (s, 3H, $C(CH_3)_2$), 1.30 (s, 3H, $C(CH_3)_2$), 1.27-1.24 (m, 8H, 4 × CH_2), 0.89 (br s, 9H, $C(CH_3)_3$), 0.07 (2x) (each s, each 3H, $Si(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7 (C, guan), 156.3 (C=O), 153.5 (C=O), 111.0 ($C(CH_3)_2$), 83.1 (^{t}Bu, Boc), 80.8 (C-3), 79.4 (^{t}Bu, Boc), 78.1 (C-2), 70.4 (C- 4), 62.1 (C-5), 60.1 (C-1), 54.7 (NCH_2), 41.2 (CH_2NH), 29.9, 29.7, 29.4, 29.1(2x) (5 × CH_2), 28.6 (Boc), 28.3 (Boc), 28.0, 27.7, 27.0 (3 × CH_2), 26.3 ($C(CH_3)_2$), 26.1(3x) ($C(CH_3)_3$), 25.5 ($C(CH_3)_2$), 18.4 ($C(CH_3)_3$), -5.2 (2x) ($Si(CH_3)_2$). HRMS (ESI-MS): *m/z* calcd for $[C_{35}H_{68}N_4O_7Si]H^+$: 685.4930, found: 685.4935.

General method for deprotection (Method C)
A solution of protected D-lyxitol in MeOH (4 mL/0.3 mmol of lyxitol) was cooled to 0 °C and 6M HCl (2 mL, 6M HCl/MeOH 1:2, v/v) was added. After 15 min, the ice-water bath was removed and the stirring was continued at rt for 16 h. The reaction mixture was neutralized with $NaHCO_3$, salts were removed by filtration,

and the solvent was evaporated. The crude product was purified by column chromatography ($CHCl_3$/MeOH/NH_3 1:0:0→10:1:0→7:1:0.1, v/v/v).

General method for deprotection (for hydrochloride) (Method D)
The solution of protected D-lyxitol in MeOH (2 mL/0.04 mmol of lyxitol) was cooled to 0 °C and 6M HCl (1 mL, 6MHCl/MeOH 1:2, v/v) was added dropwise. After 15 min, the ice-water bath was removed and the stirring was continued at rt for 16 h. The solvent was evaporated, the residue was redissolved in water (15 mL) and extracted with DCM (3 × 10 mL). Lyophilisation of the water layer afforded the target product as the hydrochloride.

***N*-Benzyl-1,4-dideoxy-1,4-imino-D-lyxitol (4)**
Deprotection of **3** (0.30 g, 0.79 mmol) was carried out following general procedure Method C. Compound **4** (121 mg, 68%), yellow oil, $[\alpha]_D$ = - 24.7 (*c* 0.39, CH_3OH); [5] $[\alpha]_D^{21}$ = - 46.2 (*c* 1.0, H_2O). ^1H NMR (600 MHz, CD_3OD): δ 7.39-7.24 (m, 5H, Ar), 4.27 (dd, 1H, *J* 5.2 Hz, *J* 7.1 Hz, H-3), 4.08 (td, 1H, *J* 3.1 Hz, *J* 5.2 Hz, H-2), 3.99 (d, 1H, *J* 13.1 Hz, NCH_2), 3.73 (dd, 1H, *J* 5.3 Hz, *J* 11.1 Hz, H-5′), 3.65 (dd, 1H, *J* 3.6 Hz, *J* 11.1 Hz, H-5), 3.54 (d, 1H, *J* 13.1 Hz, NCH_2), 2.91-2.83 (m, 2H, H-1', H-4), 2.56 (dd, 1H, *J* 5.2 Hz, *J* 10.6 Hz, H-1). ^{13}C NMR (150 MHz, CD_3OD): δ 139.7, 130.2, 129.3, 128.1 (Ar), 73.6 (C-3), 71.4 (C-2), 67.7 (C-4), 60.8 (C-5), 60.3 (NCH_2), 59.0 (C-1). HRMS: *m/z* calcd for $[C_{12}H_{17}NO_3]H^+$: 224.1281, found: 224.1284.

1,4-Dideoxy-1,4-imino-D-lyxitol hydrochloride (6)
Deprotection of **5** (46 mg, 0.16 mmol) was carried out following general procedure Method D. Compound **6** (22 mg, 82%), yellowish solid, $[\alpha]_D$ = + 19.6 (*c* 0.22, H_2O);[6] $[\alpha]_D^{27}$ = + 15.4 (*c* 0.56, H_2O);[7] $[\alpha]_D^{20}$ = + 19.8 (*c* 0.45, H_2O) ^1H NMR (400 MHz, CD_3OD): δ 4.41 (td, 1H, *J* 4.0 Hz, *J* 7.2 Hz, H-2), 4.23 (t, 1H, *J* 4.1 Hz, H-3), 3.97 (dd, 1H, *J* 4.8 Hz, *J* 11.8 Hz, H-5′), 3.91 (dd, 1H, *J* 8.7 Hz, *J* 11.8 Hz, H-5), 3.64 (dt, 1H, *J* 4.5 Hz, *J* 8.9 Hz, H-4), 3.42 (dd, 1H, *J* 7.3 Hz, *J* 11.7 Hz, H-1′), 3.17 (dd, 1H, *J* 7.1 Hz, *J* 11.7 Hz, H-1). ^{13}C NMR (100 MHz, CD_3OD): δ 71.9 (C-2), 71.4 (C-3), 64.6 (C-4), 59.4 (C-5), 48.6 (C-1). HRMS: *m/z* calcd for $[C_5H_{11}NO_3]H^+$: 134.0812, Found: 134.0814.

1,4-Dideoxy-*N*-4-guanidinomethylbenzyl-1,4-imino-D-lyxitol hydrochloride (9)
Deprotection of **8** (90 mg, 0.14 mmol) was carried out following general procedure Method C. Compound **9** (42 mg, 92%), yellow oil, $[\alpha]_D$ = + 5.6 (*c* 0.25, CH_3OH). ^1H NMR 400 MHz, CD_3OD): *δ* 7.64 (d, 2H, *J* 8.2 Hz, Ar), 7.49 (d, 2H, *J* 8.1 Hz, Ar), 4.74 (d, 1H, *J* 12.9 Hz, NCH_2), 4.52-4.49 (m, 2H, ArCH_2guan), 4.41-4.36 (m, 3H, H-2, H-3, NCH_2), 4.06 (dd, 1H, *J* 8.2 Hz, *J* 12.2 Hz, H-5′), 3.92 (dd, 1H, *J* 4.3 Hz, *J* 12.2 Hz, H-5), 3.80 (ddd, 1H, *J* 3.6 Hz, *J* 5.2 Hz, *J* 7.2 Hz, H-4), 3.43 (dd, 1H, *J* 5.7 Hz, *J* 11.8 Hz, H-1′), 3.27 (dd, 1H, *J* 4.9 Hz, *J* 11.9 Hz, H-1). ^{13}C NMR (100 MHz, CD_3OD): *δ* 158.8 (C, guan), 140.0, 132.9, 131.0, 129.1 (Ar), 72.2, 71.6, 70.5 (C-2, C-3, C-4), 60.6 (NCH_2), 59.5 (C-5), 56.9 (C-1), 45.5 (ArCH_2guan). HRMS: (ESI-MS): *m/z*: calcd for $[C_{14}H_{22}N_4O_3]H^+$: 295.1765, found: 295.1769.

1,4-Dideoxy-1,4-imino-*N*-4-iodobenzyl-D-lyxitol (16)
Deprotection of **10** (0.24 g, 0.48 mmol) was carried out following general procedure Method C. Compound **16** (0.13 g, 78%), yellow oil, $[\alpha]_D$ = - 19.6 (*c* 0.29, MeOH). ^1H NMR (400 MHz, CD_3OD): δ 7.67 (d, 2H, *J* 8.0 Hz, Ar), 7.18 (d, 2H, *J* 8.0 Hz, Ar), 4.27 (dd, 1H, *J* 4.9 Hz, *J* 7.2 Hz, H-3), 4.09 (td, 1H, *J* 3.0 Hz, *J* 5.1 Hz, H-2), 3.96 (d, 1H, *J* 13.3 Hz, NCH_2), 3.71 (dd, 1H, *J* 5.3 Hz, *J* 10.9 Hz, H-5′), 3.66 (dd, 1H, *J* 3.7 Hz, *J* 11.2 Hz, H-5), 3.50 (d, 1H, *J* 13.3 Hz, NCH_2), 2.89-2.84 (m, 2H, H-1′, H-4), 2.54 (dd, 1H, *J* 5.3 Hz, *J* 10.6 Hz, H-1). ^{13}C NMR (100 MHz, CD_3OD): δ 140.2, 138.5, 132.2, 92.9 (Ar), 73.7 (C-3), 71.6 (C-2), 67.8 (C-4), 61.0 (C-5), 59.7 (NCH_2), 59.1 (C-1). HRMS (ESI-MS): *m/z*: calcd for $[C_{12}H_{16}NO_3I]H^+$: 350.0248. Found: 350.0253.

1,4-Dideoxy-1,4-imino-*N*-(naphthalen-2-ylmethyl)-D-lyxitol (17)
Deprotection of **11** (0.14 g, 0.33 mmol) was carried out following general procedure Method C. Compound **17** (61 mg, 68%), yellow oil, $[\alpha]_D$ = - 14.5 (*c* 0.26, CH_3OH). ^1H NMR (400 MHz, CD_3OD): δ 7.86-7.82 (m, 4H, Ar), 7.56 (dd, 1H, *J* 1.7 Hz, *J* 8.4 Hz, Ar), 7.50-7.44 (m, 2H, Ar), 4.30 (dd, 1H, *J* 5.0 Hz, *J* 7.1 Hz, H-3), 4.16 (d, 1H, *J* 13.1 Hz, NCH_2), 4.10 (dt, 1H, *J* 2.6 Hz, *J* 5.1 Hz, H-2), 3.77 (dd, 1H, *J* 5.3 Hz, *J* 11.2 Hz, H-5′), 3.73-3.68 (m, 2H, NCH_2, H-5), 2.95-2.91 (m, 2H, H-1′, H-4), 2.64 (dd, 1H, *J* 5.2 Hz, *J* 10.7 Hz, H-1). ^{13}C NMR (101 MHz, CD_3OD): δ 137.6, 134.9, 134.3, 128.9, 128.7, 128.6, 128.5, 127.0, 126.7, 73.8 (C-3), 71.6 (C-2), 67.9 (C-4), 60.9 (C-5), 60.6 (NCH_2), 59.2 (C-1). HRMS (ESI-MS): *m/z*: calcd for $[C_{16}H_{19}NO_3]H^+$: 274.1438, found: 274.1441.

1,4-Dideoxy-1,4-imino-*N*-(2-(naphthalen-1-yl)ethyl)-D-lyxitol (18)
Deprotection of **12** (98 mg, 0.22 mmol) was carried out following general procedure Method C. Compound **18** (38 mg, 60%), yellow oil, $[\alpha]_D$ = - 65.1 (*c* 0.19, CH_3OH). ^1H NMR 400 MHz, CD_3OD): δ 8.12 (dd, 1H, *J* 1.0 Hz, *J* 8.5 Hz, Ar), 7.89-7.85 (m, 1H, Ar), 7.76-7.72 (m, 1H, Ar), 7.57-7.39 (m, 4H, Ar), 4.27 (dd, 1H, *J* 5.0 Hz, *J* 6.6 Hz, H-3), 4.20 (dt, 1H, *J* 3.4 Hz, *J* 5.4 Hz, H-2), 3.81 (dd, 1H, *J* 5.5 Hz, *J* 11.2 Hz, H-5′), 3.70 (dd, 1H, *J* 4.0 Hz,

J 11.2 Hz, H-5), 3.33-3.26 (m, 2H, NCH_2CH_2), 3.23 (dd, 1H, *J* 3.4 Hz, *J* 10.5 Hz, H-1′), 3.11 (ddd, 1H, *J* 7.2 Hz, *J* 9.5 Hz, *J* 12.2 Hz, NCH_2), 2.82-2.72 (m, 3H, H-1, H-4, NCH_2). ^{13}C NMR (100 MHz, CD_3OD): δ 137.4, 135.4, 133.2, 129.8, 127.9, 127.6, 127.0, 126.6, 126.5, 124.7 (Ar), 73.5 (C-3), 71.7 (C-2), 68.5 (C-4), 61.1 (C-5), 59.4 (C-1), 57.8 (NCH_2), 32.6 (NCH_2CH_2). HRMS (ESI-MS): *m/z*: calcd for $[C_{17}H_{21}NO_3]H^+$: 288.1594, found: 288.1602.

_N_-Cyclohexylmethyl-1,4-dideoxy-1,4-imino-D-lyxitol (19)
Deprotection of **13** (0.12 g, 0.31 mmol) was carried out following general procedure Method C. Compound **19** (40 mg, 55%), yellow oil, $[\alpha]_D$ = - 55.3 (*c* 0.20, MeOH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.24 (dd, 1H, *J* 5.0 Hz, *J* 7.2 Hz, H-3), 4.12 (td, 1H, *J* 3.0 Hz, *J* 5.2 Hz, H-2), 3.71 (dd, 1H, *J* 5.5 Hz, *J* 11.0 Hz, H-5′), 3.62 (dd, 1H, *J* 3.2 Hz, *J* 11.0 Hz, H-5), 3.04 (dd, 1H, *J* 3.0 Hz, *J* 10.4 Hz, H-1′), 2.66 (ddd, *J* 3.1 Hz, *J* 5.4 Hz, *J* 7.2 Hz, H-4), 2.53-2.47 (m, 2H, NCH_2, H-1), 2.26 (dd, 1H, *J* 5.0 Hz, *J* 12.1 Hz, NCH_2), 2.01-1.95 (m, 1H, Cyh), 1.78-1.69 (m, 4H, Cyh), 1.50-1.43 (m, 1H, Cyh), 1.35-1.20 (m, 3H, Cyh), 0.98-0.83 (m, 2H, Cyh). ^{13}C NMR (100 MHz, CD_3OD): δ 73.6 (C-3), 71.8 (C-2), 68.8 (C-4), 64.1 (NCH_2), 60.6 (C-5), 59.7 (C-1), 38.2 (CH), 33.1, 32.6, 27.9, 27.3, 27.1 (5 × CH_2). HRMS (ESI-MS): *m/z*: calcd for $[C_{12}H_{23}NO_3]H^+$: 230.1751. Found: 230.1760.

1,4-Dideoxy-1,4-imino-_N_-(tetrahydro-2_H_-pyran-4-yl)methyl)-D-lyxitol (20)
Deprotection of **14** (77 mg, 0.20 mmol) was carried out following general procedure Method C. Compound **20** (35 mg, 75%), yellow oil, $[\alpha]_D$ = - 28.6 (*c* 0.21, CH_3OH). ^{1}H NMR 400 MHz, CD_3OD): δ 4.25 (dd, 1H, *J* 5.0 Hz, *J* 7.1 Hz, H-3), 4.13 (dt, 1H, *J* 3.1 Hz, *J* 5.2 Hz, H-2), 3.98-3.92 (m, 2H, NCH_2), 3.72 (dd, 1H, *J* 5.4 Hz, *J* 11.0 Hz, H-5′), 3.63 (dd, 1H, *J* 3.3 Hz, *J* 11.0 Hz, H-5), 3.43 (tdd, 2H, *J* 2.3 Hz, *J* 8.4 Hz, *J* 12.0 Hz, THP), 3.05 (dd, 1H, *J* 3.1 Hz, *J* 10.3 Hz, H-1′), 2.70 (ddd, 1H, *J* 3.3 Hz, *J* 5.4 Hz, *J* 7.1 Hz, H-4), 2.58-2.51 (m, 2H, H-1, THP), 2.35 (dd, 1H, *J* 5.1 Hz, *J* 12.2 Hz, THP), 1.90-1.85 (m, 1H, THP), 1.77-1.70 (m, 1H, THP), 1.67-1.61 (m, 1H, THP), 1.29-1.19 (m, 2H, THP). ^{13}C NMR (100 MHz, CD_3OD): δ 73.6 (C-3), 71.9 (C-2), 69.0, 68.8, 68.7 (C-4, 2 × CH_2), 63.3 (CH_2), 60.8 (C-5), 59.7 (C-1), 35.5, 32.8, 32.6 (3 × CH_2). HRMS (ESI-MS): *m/z*: calcd for $[C_{11}H_{21}NO_4]H^+$: 232.1543. Found: 232.1544.

1,4-Dideoxy-_N_-dodecyl-1,4-imino-D-lyxitol (21)
Deprotection of **15** (0.14 g, 0.31 mmol) was carried out following general procedure Method C. Compound **21** (73 mg, 79%), yellowish oil, $[\alpha]_D$ = - 40.2 (*c* 0.20, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.24 (dd, 1H, *J* 5.1 Hz, *J* 6.7 Hz, H-3), 4.15 (dt, 1H, *J* 3.6 Hz, *J* 5.3 Hz, H-2), 3.80 (dd, 1H, *J* 5.8 Hz, *J* 11.0 Hz, H-5′), 3.67 (dd, 1H, *J* 3.8 Hz, *J* 11.1 Hz, H-5), 3.04 (dd, 1H, *J* 3.3 Hz, *J* 10.7 Hz, H-1′), 2.76 (dt, 1H, *J* 8.1 Hz, *J* 12.0 Hz, NCH_2), 2.69 (dd, 1H, *J* 5.9 Hz, *J* 10.4 Hz, H-4), 2.60 (dd, 1H, *J* 5.7 Hz, *J* 10.7 Hz, H-1 '), 2.40 (dt, 1H, *J* 7.5 Hz, *J* 11.9 Hz, NCH_2), 1.54-1.50 (m, 2H, CH_2), 1.31 (br s, 18H, 9 × CH_2), 0.91 (t, *J* 6.8 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, CD_3OD): δ 73.4 (C-3), 71.5 (C-2), 68.9 (C-4), 60.9 (C-5), 59.4 (C-1), 57.1 (NCH_2), 33.1, 30.8(3x), 30.7, 30.6, 30.5, 29.0, 28.6, 23.7 (10 × CH_2), 14.4 (CH_3). HRMS (ESI-MS): *m/z*: calcd for $[C_{17}H_{35}NO_3]H^+$: 302.2690, found: 302.2694.

1,4-Dideoxy-_N_-(10-guanidinodecyl)-1,4-imino-D-lyxitol hydrochloride (25)
Deprotection of **24** (28 mg, 0.04 mmol) was carried out following general procedure Method D. Compound **25** (13 mg, 88%), brownish solid, $[\alpha]_D$ = + 70.6 (*c* 0.41, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.42-4.40 (m, 1H, H-3), 4.39 (dd, 1H, *J* 4.1 Hz, 5.7 Hz, H-2), 4.06-4.01 (m, 2H, H-5, H-5′), 3.66-3.62 (m, 1H, H-4), 3.54-3.48 (m, 2H, NCH_2, H-1′), 3.38 (dd, 1H, *J* 5.7 Hz, *J* 12.0 Hz, H-1), 3.21-3.16 (m, 3H, NCH_2, CH_2NH), 1.80-1.72 (m, 2H, CH_2), 1.65-1.58 (m, 2H, CH_2), 1.39 (br s, 14H, 7 × CH_2). ^{13}C NMR (101 MHz, CD_3OD): δ 158.5 (C, guan), 72.2, 72.0, 70.7 (C-2, C-3, C-4), 59.7 (C-5), 58.1 (NCH_2), 57.6 (C-1), 42.5 (CH_2NH), 30.5(2x), 30.3, 30.2, 29.9, 27.7(2x), 26.2 (8 × CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{16}H_{34}N_4O_3]H^+$: 331.2704, found: 331.2706.

_N_-(9-amidinononyl)-1,4-dideoxy-1,4-imino-D-lyxitol hydrochloride (26)
Nitrile **22** (71.7 mg, 0.16 mmol) was dissolved in anhydrous ether (5 mL) and LiHMDS (0.20 g, 1.21 mmol) was added. The mixture was sonicated at 40 °C for 2 h under inert atmosphere. The solvent was evaporated and the residue was stirred with water (10 mL) for 30 min. The water layer was extracted with DCM (3 × 10 mL), the combined organic phases were washed with brine (30 mL), dried (Na_2SO_4) and concentrated to give the crude amidine (61.6 mg) which was used in the next step without purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.62-4.56 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.2 Hz, *J* 10.1 Hz, H-5′), 3.74 (dd, 1H, *J* 5.3 Hz, *J* 10.2 Hz, H-5), 3.20 (d, 1H, *J* 11.0 Hz, H-1′), 2.90 (m, 1H, NCH_2), 2.21 (q, 1H, *J* 5.6 Hz, H-4), 2.01-1.97 (m, 2H, H-1, NCH_2), 1.67-1.28 (m, 16H, 8 × CH_2), 1.47 (s, 3H, $C(CH_3)_2$), 1.29 (s, 3H, $C(CH_3)_2$), 0.90 (br s, 9H, $C(CH_3)_3$), 0.07(2x) (each s, each 3H, $Si(CH_3)_2$). Deprotection of the crude amidine (61 mg) was carried out following general procedure Method D. Compound **26** (43 mg, 95%), brownish oil, $[\alpha]_D$ = + 31.0 (*c* 0.41, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ 4.43-4.36 (m, 2H, H-2, H-3), 4.03-4.00 (m, 2H, H-5, H-5′), 3.66-3.61 (m, 1H, H-4), 3.51-3.47 (m, 2H, NCH_2, H-1′), 3.37-3.33 (m, 1H, H-1), 3.15-3.08 (m, 1H, NCH_2), 1.75-1.30 (m, 16H, 8 × CH_2). ^{13}C NMR (100 MHz,

CD_3OD): δ 163.3 (C, amidine), 72.0, 70.8, 70.5 (C-2, C-3, C-4), 59.5 (C-5), 57.9 (NCH_2), 57.4 (C- 1), 30.1(2x), 29.9(2x), 29.8(2x), 27.4, 25.9 (8 × CH_2). HRMS (ESI-MS): *m/z* calcd for $[C_{15}H_{31}N_3O_3]H^+$: 302.2438, found: 302.2441.

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