SUPPORTING INFORMATION

Synthesis and Biological Investigation of

Δ^{12} -Prostaglandin J₃ (Δ^{12} -PGJ₃) Analogs and Related Compounds

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I. Schemes for the Synthesis of Analogs 40–44

Scheme S1: Synthesis of Δ^{12} -PGJ₃ Analogs 40 and 41.^{*a*}



^aReagents and conditions: (a) LiBH₄ (2.0 M in THF, 2.0 equiv), THF, o to $25 \,^{\circ}$ C, 12 h; (b) TBSCl (1.5 equiv), Et₃N (3.0 equiv), DMAP (0.1 equiv), CH₂Cl₂, 3 h, 62 % for two steps; (c) TEMPO (0.05 equiv), NalO₄-SiO₂ (2.0 equiv), CH₂Cl₂, 4 h, 84%; d) LDA (2.0 equiv), THF, -78 °C; then **150** (1.0 equiv); then **58** (1.2 equiv), 30 min; e) MsCl (5.0 equiv), Et₃N (10 equiv), CH₂Cl₂, o °C, 5 min; (f) Al₂O₃ (21 equiv), CH₂Cl₂, 25 °C, 8 h, 57% for 3 steps; (g) HF (50% aq., 50 equiv), MeCN, o °C, 1 h, 99%; (h) LDA (2.0 equiv), THF, -78 °C; then **150** (1.0 equiv); then **64** (1.2 equiv), 15 min; (i) MsCl (2.0 equiv), DMAP (10 equiv), CH₂Cl₂, o to 25 °C, 6 h, 34 % for two steps; (j) HF (50% aq., 50 equiv), MeCN, o °C, 45 min, 87 %. TBSCl = *tert*-butyldimethylsilyl chloride, TEMPO = 2,2,6,6-tetramethylpiperidin-1-yl)oxyl, LDA = lithium diisopropylamide, MsCl = methanesulfonyl chloride, DMAP = 4-dimethylaminopyridine.

Scheme S2: Synthesis of Δ¹²-PGJ₃ Analogs 42 and 43.^{*a*}



^aReagents and conditions: (a) $Co_2(CO)_8$ (1.0 equiv), pentane, 0 °C, 2 h, quant.; (b) NMO·H₂O (6.1 equiv), vinyl benzoate (65 equiv), CH₂Cl₂, 25 °C, 15 h, 62 % for two steps; (c) LDA (1.1 equiv), THF, -78 °C; then **157** (1.0 equiv), then **58** (1.0 equiv), 30 min; d) MsCl (5.0 equiv), Et₃N (10 equiv), CH₂Cl₂, 0 °C, 1 h; (e) Al₂O₃ (10 equiv), CH₂Cl₂, 25 °C, 16 h, 40% for three steps; (f) HF (50 % aq., 30 equiv), MeCN, 0 °C, 10 min, 39 %; (g) LDA (1.1 equiv), THF, -78 °C; then **157** (1.0 equiv), then **64** (1.0 equiv), 30 min; (h) MsCl (1.1 equiv), Et₃N (2.2 equiv), CH₂Cl₂, -10 °C, 1 h; (i) Al₂O₃ (10 equiv), CH₂Cl₂, 25 °C, 16 h, 23% for three steps; (j) HF (50 % aq., 30 equiv), MeCN, 0 °C, 10 min, 70 %. NMO = 4-methylmorpholine *N*-oxide.

Scheme S3: Synthesis of PGJ₂ lactone 44.^{*a*}



^{*a*}Reagents and conditions: (a) H₂, Pd/C, MeOH, 24 h, 63%; (b) DMP (2.0 equiv), CH₂Cl₂, 25 °C, 90 min, 84%; (c) MNBA (2.0 equiv), DMAP (6.0 equiv), CH₂Cl₂, 25 °C, 17 h; 72 %. DMP = Dess-Martin periodinane, MNBA = 2-methyl-6-nitrobenzoic anhydride.

II. General Methods

All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene, diethyl ether (Et₂O), acetonitrile (MeCN), methylene chloride (CH₂Cl₂), triethylamine (Et₃N), diisopropylamine, and pyridine were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (¹H-NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F₂₅₄) using UV light as visualizing agent and an ethanolic solution of phosphomolybdic acid and cerium sulfate or an aqueous solution of potassium permanganate and heat as developing agents. Acros Organics silica gel (60 Å, particle size 0.035–0.070 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.25 mm E. Merck silica gel plates (60F₂₅₄). NMR spectra were recorded on a Bruker Avance III HD 600 MHz equipped with a 5 mm DCH cryoprobe, a Bruker Avance III 500 MHz, and a Bruker 400 MHz instrument, calibrated using residual undeuterated solvent for ¹H-NMR [$\delta_{\rm H}$ = 7.26 (CHCl₃), 7.16 (C₆D₅H), and 2.50 (DMSO-*d*₅) ppm] and deuterated solvent for ¹³C-NMR [$\delta_C = 77.16$ (CDCl₃), 128.06 (C₆D₆), and 39.52 (DMSO-d₆) ppm] as an internal reference at 298 K. The following abbreviations were used to indicate the multiplicities: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septet, and m = multiplet. IR spectra were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrometer. High-resolution mass spectra (HR-MS) were recorded on an Agilent Ion Trap-Time of Flight Mass Spectrometer operated with an ESI (electrospray ionization) source interface. Optical rotations were measured on a Schmidt+HaenschPolartronic M100 polarimeter at 589.44 nm using 100 mm cells and the solvent and concentration indicated [in units of 10^{-1} (deg cm² g⁻¹)]. UV-vis spectra were recorded on a Varian Cary 5000 UV-vis-NIR-spectrometer and a Beckman DU 7500 spectrophotometer using 10 mm quartz-cells and the solvent and concentration indicated.

III. Experimental Procedures and Physical Data of Compounds

Synthesis of Δ^{12} -PGJ₃ Methyl Ester (2) and Lactone (11):

Methyl (5Z,12E,15S,17Z)-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oate (2): To a stirred



solution of Δ^{12} -PGJ₃ (1)¹ (5.0 mg, 15 µmol, 1.0 equiv) in C₆H₆:MeOH (3:2, 0.5 mL) at 25 °C was dropwise added a solution of trimethylsilyl diazomethane (2 M in Et₂O, 12 µL, 23 µmol, 1.5 equiv) (yellow color

persists). After stirring for 30 min, the reaction mixture was concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, $2:1\rightarrow3:2$) yielded pure title compound (**2**, 4.9 mg, 14 µmol, 93 % yield) as a colorless oil.

2: $R_f = 0.53$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{25} = +206.3$ (c = 0.4 in C₆H₆); IR (film): $v_{max} = 3446$, 3009, 2956, 2927, 2872, 2855, 1736, 1700, 1651, 1579, 1436, 1208, 1049 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ 7.51 (ddd, J = 6.0, 2.7, 1.0 Hz, 1 H), 6.65 - 6.62 (m, 1 H), 6.34 (dd, J = 6.0, 1.8 Hz, 1 H), 5.62 - 5.57 (m, 1 H), 5.49 - 5.43 (m, 1 H), 5.40 - 5.33 (m, 2 H), 3.84 (quint, J = 6.4 Hz, 1 H), 3.66 (s, 3 H), 3.50 (ddd, J = 6.6, 3.9, 2.0 Hz, 1 H), 2.66 - 2.61 (m, 1 H), 2.56 - 2.43 (m, 2 H), 2.31 - 2.19 (m, 5 H), 2.09 - 2.01 (m, 4 H), 1.98 (brs, 1 H), 1.67 (quint, J = 7.4 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (125 MHz, CDCl₃) δ 196.50, 174.17, 161.81, 139.49, 135.87, 135.08, 131.79, 131.67, 125.95, 123.85, 70.64, 51.73, 43.45, 36.66, 35.00, 33.48, 30.41, 26.83, 24.77, 20.90, 14.37 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₃₀O₄Na [M+Na]⁺: 369.2036, found: 369.2046.

(5Z,12E,15S,17Z)-1,15-Epoxyprosta-5,9,12,17-tetraene-1,11-dione (11): To a stirred solution



of 2-methyl-6-nitrobenzoic anhydride (15 mg, 42 µmol, 1.4 equiv) and 4-dimethylaminopyridine (22 mg, 180 µmol, 6.0 equiv) in CH₂Cl₂ (20 mL) was added a solution of Δ^{12} -PGJ₃ (**1**) (10 mg, 30 µmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at 25 °C dropwise via syringe pump over 15 h. After stirring for an

additional 2 h, the reaction mixture was washed sequentially with sat. aq. NaHCO₃-solution (10 mL), aq. HCl (0.2 M, 10 mL), and brine (10 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 3:1) yielded pure title compound (**11**, 7.0 mg, 22 μ mol, 74 % yield) as a white solid.

11: $R_f = 0.35$ (hexanes:EtOAc, 3:1); mp = 62-65 °C; $[\alpha]_D^{25} = +65.2$ (c = 0.6 in C_6H_6); IR (film): $v_{max} = 3010, 2961, 2927, 2855, 1727, 1704, 1655, 1581, 1456, 1440, 1239, 1151, 1024$ cm⁻¹;

¹H-NMR (600 MHz, C₆D₆) δ 6.81 (ddd, J = 6.1, 2.7, 1.0 Hz, 1 H), 6.59 (dd, J = 11.7, 4.4 Hz, 1 H), 6.19 (dd, J = 6.1, 1.9 Hz, 1 H), 5.49 – 5.43 (m, 1 H), 5.30 – 5.26 (m, 1 H), 5.19 – 5.14 (m, 1 H), 5.13 – 5.05 (m, 2 H), 3.21 – 3.18 (m, 1 H), 2.54 (ddd, J = 14.6, 9.7, 5.2 Hz, 1 H), 2.39 – 2.27 (m, 3 H), 2.23 – 2.18 (m, 1 H), 2.11 – 1.92 (m, 6 H), 1.81 – 1.76 (m, 1 H), 1.30 – 1.25 (m, 2 H), 0.88 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 194.78, 172.28, 159.81, 140.31, 135.57, 134.99, 131.82, 130.85, 125.40, 123.52, 72.82, 43.21, 33.70, 32.82, 32.13, 28.44, 26.05, 24.65, 21.03, 14.37 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₇O₃ [M+H]⁺: 315.1955, found: 315.1955.

Synthesis of Δ^{12} -PGJ₃ Ester Analogs 3–5 and 10:

Isopropyl (5*Z*,12*E*,15*S*,17*Z*)-15-{[*tert*-butyl(dimethyl)silyl]oxy}-11-oxoprosta-5,9,12,17tetraen-1-oate (46): To a stirred solution of carboxylic acid 45¹ (30 mg, 67 μmol, 1.0 equiv) in



CH₂Cl₂ (1 mL) at 0 °C was added EDCI (23 mg, 130 μ mol, 2.0 equiv) and DMAP (0.39 mg, 3.3 μ mol, 0.05 equiv). After stirring for 20 min at this temperature, *iso*-propyl alcohol (10 μ L,

40 µmol, 1.5 equiv) was added. After stirring the resulting solution for an additional 6 h at 0 °C, the reaction mixture was quenched with saturated aqueous NH₄Cl-solution (5 mL) and diluted with CH₂Cl₂ (5 mL). The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 5 mL), and the combined organic extracts were washed with brine (5 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 9:1→3:1→3:2) gave pure title compound (**46**, 26 mg, 0.053 mmol, 79 % yield) as a colorless oil.

46: $R_f = 0.60$ (hexanes: EtOAc, 3:2); $[\alpha]_D^{25} = +127.5$ (c = 1.0 in CHCl₃); IR (film): $v_{max} = 3012$, 2956, 2930, 2857, 1731, 1706, 1654, 1462, 1251, 1088, 835, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.49 (dd, J = 6.0, 2.6 Hz, 1 H), 6.60 (t, J = 8.2 Hz, 1 H), 6.32 (dd, J = 6.0, 1.8 Hz, 1 H), 5.49 – 5.45 (m, 2 H), 5.39 – 5.35 (m, 2 H), 5.00 (sept, J = 6.3 Hz, 1 H), 3.89 (quint, J = 6.0 Hz, 1 H), 3.45 (ddd, J = 8.0, 3.8, 1.8 Hz, 1 H), 2.64 – 2.40 (m, 1 H), 2.45 – 2.40 (m, 2 H), 2.29 – 2.13 (m, 5 H), 2.06 – 1.95 (m, 4 H), 1.66 (quint, J = 7.2 Hz, 2 H), 1.22 (d, J = 6.3 Hz, 6 H) 0.94 (t, J = 7.5 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.35, 173.08, 161.57, 138.83, 135.05, 134.12, 132.66, 131.61, 126.12, 124.41, 71.68, 67.63, 43.47, 36.91, 35.30, 34.19, 30.65, 26.85, 25.97, 24.92, 21.99, 20.89, 18.20, 14.31, -4.43 ppm; HR-MS (ESI-TOF): calcd for C₂₉H₄₈O₄SiNa [M+Na]⁺: 511.3204, found: 511.3214.

Isopropyl (5Z,12E,15S,17Z)-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oate (3): To a



stirred solution of carboxylic acid **46** (10 mg, 20 μ mol, 1.0 equiv) in CH₂Cl₂ (1 mL) at 0 °C was dropwise added a solution of HF:NEt₃ (190 μ L, 1.0 mmol, 50 equiv) in CH₂Cl₂ (0.5 mL). After stirring for

48 h at room temperature, the reaction mixture was quenched by addition of saturated brine (3 mL) and extracted with EtOAc (5 × 10 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 3:1 \rightarrow 3:2) gave pure title compound (**3**, 6.1 mg, 16 µmol, 80 % yield) as a colorless oil.

3: $R_f = 0.20$ (hexanes:EtOAc, 3:2); $[\alpha]_D^{25} = +158.2$ (c = 0.5 in C_6H_6); IR (film): $v_{max} = 3449$, 2963, 2933, 1728, 1708, 1651, 1456, 1374, 1216, 1180, 1109, 531 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 6.94 (dd, J = 6.2, 2.4 Hz, 1 H), 6.84 (t, J = 7.5 Hz, 1 H), 6.20 (dt, J = 6.1, 1.5 Hz, 1 H), 5.51 – 5.47 (m, 1 H), 5.39 – 5.35 (m, 1 H), 5.31 – 5.27 (m, 1 H), 5.21 – 5.17 (m, 1 H), 5.01 (sept, J = 6.2 Hz, 1 H), 3.54 (quint, J = 6.2 Hz, 1 H), 3.12 – 3.10 (m, 1 H), 2.43 (dt, J = 14.4, 5.3 Hz, 1 H), 2.31 (dt, J = 14.7, 7.3 Hz, 1 H), 2.24 – 2.02 (m, 6 H), 1.92 (quint, J = 7.5 Hz, 2 H), 1.89 (q, J = 7.5 Hz, 2 H), 1.56 (quint, J = 7.4 Hz, 2 H), 1.05 (d, J = 6.3 Hz, 6 H), 0.89 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 194.83, 172.23, 160.20, 139.17, 134.86, 134.31, 131.40, 131.17, 125.97, 124.50, 70.22, 67.08, 43.06, 36.54, 35.01, 33.62, 30.20, 26.57, 24.73, 21.50, 20.70, 14.05 ppm; HR-MS (ESI-TOF): calcd for $C_{23}H_{34}O_4$ Na [M+Na]⁺: 397.2349, found: 397.2344.

Decyl $(5Z,12E,15S,17Z)-15-{[$ *tert* $-butyl(dimethyl)silyl]oxy}-11-oxoprosta-5,9,12,17-tetraen-$ 1-oate (47): To a stirred solution of carboxylic acid 45¹ (27 mg, 60 µmol, 1.0 equiv) in CH₂Cl₂



(1 mL) at 0 °C was added EDCI (23 mg, 120 μ mol, 2.0 equiv) and DMAP (0.36 mg, 3.0 μ mol, 0.05 equiv). After stirring for 20 min at this temperature, was added decyl alcohol (23 μ L, 120 μ mol,

2.0 equiv). After stirring the resulting solution for an additional 12 h at 25 °C, the reaction mixture was quenched with saturated aqueous NH₄Cl-solution (5 mL) and diluted with CH₂Cl₂ (5 mL). The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2×5 mL), and the combined organic extracts were washed with brine (10 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography

(SiO₂, hexanes:EtOAc, 9:1 \rightarrow 4:1) gave pure title compound (47, 26 mg, 0.045 mmol, 76% yield) as a colorless oil.

47: $R_f = 0.30$ (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = +117.0$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 3009$, 2955, 2927, 2856, 1735, 1707, 1658, 1462, 1251, 1088, 836, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.48 (ddd, J = 6.0, 2.6, 1.0 Hz, 1 H), 6.60 (t, J = 8.2 Hz, 1 H), 6.32 (dd, J = 6.0, 1.8 Hz, 1 H), 5.50 – 5.44 (m, 2 H), 5.39 – 5.34 (m, 2 H), 4.05 (t, J = 6.8 Hz, 2 H), 3.89 (quint, J = 6.0 Hz, 1 H), 3.45 (ddd, J = 8.9, 4.1, 2.1 Hz, 1 H), 2.63 – 2.59 (m, 1 H), 2.44 – 2.41 (m, 2 H), 2.29 – 2.14 (m, 5 H), 2.05 – 1.96 (m, 4 H), 1.67 (quint, J = 7.5 Hz, 2 H), 1.62 – 1.55 (m, 2 H), 1.37 – 1.21 (m, 14 H), 0.94 (t, J = 7.5 Hz, 3 H), 0.89 – 0.85 (m, 12 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.29, 173.59, 161.52, 135.06, 134.97, 134.11, 134.04, 132.65, 132.57, 131.55, 126.12, 124.40, 71.68, 71.57, 64.62, 43.43, 36.87, 35.26, 33.81, 31.97, 30.64, 30.57, 29.61, 29.38, 28.74, 26.82, 26.01, 25.87, 24.85, 22.76, 20.85, 18.15, 14.26, 14.19, -4.45, -4.49 ppm; HR-MS (ESI-TOF): calcd for C₃₆H₆₂O₄SiNa [M+Na]⁺: 609.4310, found: 609.4297.

Decyl (52,12E,155,17Z)-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oate (4): To a stirred



solution of decyl ester **47** (20 mg, 34 μ mol, 1.0 equiv) in MeCN (1 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 140 μ L, ca. 3.4 mmol, ca. 100 equiv) in MeCN (0.5 mL). After

stirring for 30 min at this temperature, the reaction mixture was quenched with brine (3 mL) and extracted with EtOAc (5×5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 3:2) gave pure title compound (**4**, 13 mg, 27 µmol, 79 % yield) as a colorless oil.

4: $R_f = 0.20$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = +116.8$ (c = 0.50 in C_6H_6); IR (film): $v_{max} = 3445$, 2925, 2856, 1734, 1703, 1654, 1457, 1179, 1179, 1053, 1033, 804, 723 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 6.94 (ddd, J = 6.0, 2.6, 0.9 Hz, 1 H), 6.83 (t, J = 7.6 Hz, 1 H), 6.21 (dd, J = 6.0, 1.8 Hz, 1 H), 5.49 (dtt, J = 10.5, 7.2, 1.6 Hz, 1 H), 5.38 – 5.27 (m, 2 H), 5.22 – 5.17 (m, 1 H), 4.05 (t, J = 6.7 Hz, 2 H), 3.50 (quint, J = 7.0 Hz, 1 H), 3.12 (ddq, J = 8.7, 4.2, 2.0 Hz, 1 H), 2.44 (dddd, J = 14.4, 6.2, 4.2, 1.5 Hz, 1 H), 2.30 (dt, J = 14.7, 7.3 Hz, 1 H), 2.21 (ddd, J = 14.7, 8.0, 5.4 Hz, 1 H), 2.17 – 2.01 (m, 5 H), 2.00 – 1.86 (m, 4 H), 1.58 (quint, J = 7.0 Hz, 3 H), 1.54 – 1.45 (m, 2 H), 1.35 – 1.15 (m,

14 H), 0.92 (t, J=7.1 Hz, 3 H), 0.89 (t, J=7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 195.03, 173.13, 160.40, 139.60, 135.29, 134.77, 131.57, 126.39, 124.82, 70.60, 64.59, 43.44, 36.91, 35.35, 33.68, 32.32, 30.62, 29.97, 29.77, 29.67, 29.15, 26.97, 26.35, 25.11, 23.13, 21.08, 14.43, 14.39 ppm; HR-MS (ESI-TOF): calcd for C₃₀H₄₈O₄Na [M+Na]⁺: 495.3445, found: 495.3460.

Icosyl (5Z,12E,15S,17Z)-15-{[*tert*-butyl(dimethyl)silyl]oxy}-11-oxoprosta-5,9,12,17-tetraen-1-oate (48): To a stirred solution of carboxylic acid 45¹ (27 mg, 0.060 mmol, 1.0 equiv) in CH₂Cl₂



(1 mL) at 0 °C was added EDCI (23 mg, 120 μ mol, 2.0 equiv) and DMAP (360 μ g, 3.0 μ mol, 0.05 equiv). After stirring for 20 min at this temperature, alcohol (36 mg, 120 μ mol, 2.0 equiv) was added.

After stirring the resulting solution for an additional 12 h at 25 °C, the reaction mixture was quenched with saturated aqueous NH₄Cl-solution (5 mL) and diluted with CH₂Cl₂ (5 mL). The phases were separated, the aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 9:1 \rightarrow 4:1) gave pure title compound (48, 31 mg, 0.042 mmol, 71 % yield) as a colorless oil. **48**: $R_f = 0.36$ (hexanes: EtOAc, 4:1); $[\alpha]_D^{25} = +88.2$ (*c* = 1.0 in C₆H₆); IR (film): $v_{max} = 3008$, 2925, 2854, 1736, 1707, 1659, 1582, 1463, 1212, 1251, 1088, 836, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.48 (ddd, J=6.0, 2.6, 1.0 Hz, 1 H), 6.60 (t, J=8.2 Hz, 1 H), 6.32 (dd, J=6.0, 1.8 Hz, 1 H), 6.34 (dd, J=6.0, 1 H), 5.49 – 5.44 (m, 2 H), 5.39 – 5.34 (m, 2 H), 4.04 (t, J=6.8 Hz, 2 H), 3.89 (quint, J=6.0 Hz, 1 H), 3.45 (ddt, J=8.8, 4.0, 2.0 Hz, 1 H), 2.65 – 2.58 (m, 1 H), 2.44 – 2.40 (m, 2 H), 2.29 – 2.14 (m, 5 H), 2.05 - 1.97 (m, 4 H), 1.67 (quint, J=7.5 Hz, 2 H), 1.62 - 1.58 (m, 2 H), 1.33 - 1.23 (m, 2 H), 1.34 (m, 234 H), 0.94 (t, J=7.5 Hz, 3 H), 0.88 – 0.85 (m, 12 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.27, 173.58, 161.50, 138.78, 134.97, 134.04, 132.64, 131.48, 126.05, 124.40, 71.68, 64.62, 43.43, 36.87, 35.26, 33.80, 32.01, 30.64, 29.79, 29.40, 28.74, 26.82, 25.87, 24.85, 22.78, 20.85, 18.15, 14.28, 14.20, -4.45, -4.49 ppm; HR-MS (ESI-TOF): calcd for C₄₆H₈₂O₄SiNa [M+Na]⁺: 749.5875, found: 749.5854.

Icosyl (5Z,12E,15S,17Z)-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oate (5): To a stirred



solution of TBS ether **48** (20.0 mg, 27.5 μ mol, 1.0 equiv) in MeCN (1 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 110 μ L, ca. 2.75 mmol, ca. 100 equiv) in MeCN (0.5 mL). After

stirring for 30 min at this temperature, the reaction mixture was quenched with brine (3 mL) and extracted with EtOAc (5×5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 3:2) gave pure title compound (**5**, 12.8 mg, 20.9 µmol, 76% yield) as a colorless oil.

5: $R_f = 0.40$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +101.0$ (c = 0.5 in C₆H₆); IR (film): $v_{max} = 3410$, 2917, 2850, 1735, 1700, 1651, 1467, 1178, 1048, 803, 721 cm⁻¹; ¹H-NMR (600 MHz, C₆D₆) δ 6.94 (dd, J = 6.2, 2.6 Hz, 1 H), 6.83 (t, J = 7.6 Hz, 1 H), 6.21 (dd, J = 6.1, 1.8 Hz, 1 H), 5.50 (dtt, J = 10.5, 7.2, 1.6 Hz, 1 H), 5.38 – 5.27 (m, 1 H), 5.25 – 5.16 (m, 1 H), 4.06 (t, J = 6.7 Hz, 2 H), 3.51 (p, J = 6.3, 5.7 Hz, 1 H), 3.12 – 3.10 (m, 1 H), 2.49 – 2.39 (m, 1 H), 2.30 (dt, J = 14.7, 7.3 Hz, 1 H), 2.21 (ddd, J = 14.7, 8.1, 5.4 Hz, 1 H), 2.17 – 2.01 (m, 5 H), 2.00 – 1.87 (m, 4 H), 1.59 (quint, J = 7.3 Hz, 3 H), 1.51 (quint, J = 6.9 Hz, 2 H), 1.36 – 1.19 (m, 34 H), 0.92 – 0.97 (m, 6 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 195.01, 173.13, 160.39, 139.61, 135.30, 134.78, 131.55, 131.52, 126.40, 124.81, 70.60, 64.59, 43.44, 36.91, 35.35, 33.68, 30.62, 30.24, 30.22, 30.16, 30.08, 30.02, 29.86, 29.16, 26.97, 26.37, 25.11, 23.15, 21.08, 14.44, 14.40 ppm; HR-MS (ESI-TOF): calcd for C₄₀H₆₈O₄Na [M+Na]⁺: 635.5010, found: 635.4991.

2-(Phenylsulfonyl)ethyl (5Z,12E,15S,17Z)-15-{[*tert*-butyl(dimethyl)silyl]oxy}-11-oxoprosta-5,9,12,17-tetraen-1-oate (49): To a stirred solution of carboxylic acid 45¹ (31 mg, 69 μmol,



1.0 equiv) in CH₂Cl₂ (1 mL) at 0 °C was added EDCI (20 mg, 100 μ mol, 1.5 equiv) and DMAP (0.40 mg, 3.4 μ mol, 0.05 equiv). After stirring for 20 min at this temperature, PhSO₂(CH₂)₂OH (19 mg,

100 μ mol, 1.5 equiv) was added. After stirring the resulting solution for an additional 6 h at 0 °C, the reaction mixture was quenched with saturated aqueous NH₄Cl-solution (5 mL) and diluted with CH₂Cl₂ (5 mL). The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 5 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography

(SiO₂, hexanes:EtOAc, 3:2) gave pure title compound (**49**, 36 mg, 0.059 mmol, 86 % yield) as a colorless oil.

49: $R_f = 0.60$ (hexanes:EtOAc, 2:3); $[\alpha]_D^{25} = +114.8$ (c = 0.45 in C_6H_6); IR (film): $v_{max} = 3008$, 2956, 2929, 2856, 1740, 1702, 1655, 1462, 1447, 1323, 1251, 1086, 836 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.93 – 7.91 (m, 2 H), 7.67 (tt, J = 7.4, 1.1 Hz, 1 H), 7.58 (t, J = 7.5 Hz, 2 H), 7.47 (dd, J = 6.1, 2.7 Hz, 1 H), 6.60 (t, J = 7.6 Hz, 1 H), 6.32 (dd, J = 6.0, 1.8 Hz, 1 H), 5.49 – 5.44 (m, 1 H), 5.43 – 5.34 (m, 3 H), 4.40 (t, J = 6.2 Hz, 2 H), 3.88 (quint, J = 6.2 Hz, 1 H), 3.45 (t, J = 6.2 Hz, 3 H), 2.59 (dt, J = 14.4, 5.4 Hz, 1 H), 2.46 – 2.37 (m, 2 H), 2.28 – 2.15 (m, 3 H), 2.07 (t, J = 7.6 Hz, 2 H), 2.03 – 1.94 (m, 4 H), 1.54 (quint, J = 7.5 Hz, 2 H), 0.94 (t, J = 7.5 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.33, 172.80, 161.50, 139.59, 138.79, 135.10, 134.16, 134.07, 132.70, 131.24, 129.49, 128.26, 126.33, 124.39, 71.67, 57.60, 55.17, 43.38, 36.91, 35.30, 33.23, 30.63, 26.69, 25.97, 24.47, 20.89, 18.20, 14.31, -4.43 ppm; HR-MS (ESI-TOF): calcd for C₃₄H₅₀O₆SSiNa [M+Na]: 637.2994, found: 637.2982.

2-(Phenylsulfonyl)ethyl (5Z,12E,15S,17Z)-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-

oate (10): To a stirred solution of dienone sulfonate ester **49** (4.0 mg, 6.5 μ mol, 1.0 equiv) in $\int_{O}^{O} \int_{O}^{O} \int_{O}^{Ph} MeCN (1 \text{ mL}) \text{ at } 0 \,^{\circ}\text{C}$ was dropwise added a solution of HF (50% aq., 13 μ L, ca. 0.32 mmol, ca. 50 equiv) in MeCN (0.5 mL). After stirring for 30 min at this temperature, the reaction mixture was quenched with brine (3 mL) and extracted with EtOAc (5 × 5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and

concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 2:3) gave pure title compound (**10**, 2.4 mg, 4.9 μ mol, 76% yield) as a colorless oil.

10: $R_f = 0.20$ (hexanes: EtOAc, 2:3); $[\alpha]_D^{25} = +99.3$ (c = 0.20 in CHCl₃); IR (film): $v_{max} = 3425$, 2925, 1738, 1697, 1651, 1447, 1321, 1142, 1085, 726 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.93 – 7.91 (m, 2 H), 7.67 (tt, J = 7.4, 1.1 Hz, 1 H), 7.58 (t, J = 7.5 Hz, 2 H), 7.49 (dd, J = 6.1, 2.7 Hz, 1 H), 6.63 (t, J = 7.6 Hz, 1 H), 6.34 (dd, J = 6.0, 1.8 Hz, 1 H), 5.62 – 5.57 (m, 1 H), 5.43 – 5.34 (m, 3 H), 4.41 (t, J = 6.2 Hz, 2 H), 3.88 – 3.82 (m, 1 H), 3.52 – 3.50 (m, 1 H), 3.45 (t, J = 6.3 Hz, 2 H), 2.61 (dt, J = 14.4, 5.4 Hz, 1 H), 2.54 – 2.43 (m, 2 H), 2.28 (t, J = 6.8 Hz, 2 H), 2.23 (dt, J = 15.6, 7.2 Hz, 1 H), 2.10 – 2.03 (m, 4 H), 1.97 (q, J = 7.7 Hz, 2 H), 1.90 (d, J = 4.4 Hz, 1 H), 1.55 (quint, J = 6.8 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.43, 172.93, 161.70, 139.56,

139.48, 135.91, 135.11, 134.10, 131.80, 131.44, 129.51, 128.26, 126.08, 123.82, 70.66, 57.61, 55.17, 43.35, 36.66, 35.05, 33.19, 30.39, 26.69, 24.43, 20.89, 14.34 ppm; HR-MS (ESI-TOF): calcd for C₂₈H₃₆O₆SNa [M+Na]⁺: 523.2125, found: 521.2122.

Synthesis of Δ^{12} -PGJ₃ Amide Analogs 6–9:

(5Z,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-11-oxoprosta-5,9,12,17-tetraen-1-

amide (50): To a stirred solution of carboxylic acid 45¹ (45 mg, 0.10 mmol, 1.0 equiv) in CH₂Cl₂



(1 mL) at 0 °C was added Boc₂O (56.7 mg, 0.26 mmol, 2.6 equiv) and ammonium bicarbonate (19 mg, 0.24 mmol, 2.4 equiv). After stirring for 5 min at this temperature, pyridine (97 µL, 0.12 mmol, 1.2 equiv)

was added. The resulting solution was slowly warmed to 25 °C and stirring was continued at the same temperature for an additional 6 h. The reaction mixture was then quenched with saturated aqueous NH₄Cl-solution (10 mL) and diluted with CH₂Cl₂ (15 mL). The phases were separated and the aqueous layer was extracted with CH₂Cl₂ (2×15 mL). The combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:4) gave pure title compound (**50**, 31 mg, 0.068 µmol, 68 % yield) as a colorless oil.

50: $R_f = 0.40$ (hexanes:EtOAc, 1:4); $[\alpha]_D^{25} = +142.6$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 3347$, 3198, 3009, 2955, 2930, 2857, 1698, 1655, 1461, 1253, 1060, 1033, 836, 775 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 7.02 (dd, J = 6.2, 2.5 Hz, 1 H), 6.84 (t, J = 7.6 Hz, 1 H), 6.27 (s, 1 H), 6.23 (dd, J = 6.0, 1.8 Hz, 1 H), 5.53 – 5.43 (m, 2 H), 5.37 – 5.33 (m, 1 H), 5.26 – 5.20 (m, 1 H), 4.88 (s, 1 H), 3.79 (quint, J = 6.0 Hz, 1 H), 3.19 – 3.18 (m, 1 H), 2.44 (dt, J = 14.6, 5.7 Hz, 1 H), 2.39 – 2.36 (m, 2 H), 2.29 – 2.19 (m, 2 H), 2.10 (dt, J = 14.8, 8.4 Hz, 1 H), 2.01 – 1.89 (m, 4 H), 1.83 (t, J = 7.3 Hz, 2 H), 1.58 (quint, J = 7.0 Hz, 2 H), 0.97 (s, 9 H), 0.91 (t, J = 7.5 Hz, 3 H), 0.10 (s, 3 H), 0.07 (s, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 195.29, 174.83, 160.87, 139.33, 135.22, 134.10, 131.95, 131.87, 126.16, 124.88, 71.98, 43.48, 37.03, 35.63, 34.93, 30.83, 27.03, 26.13, 25.46, 21.16, 18.32, 14.44, -4.32, -4.35 ppm; HR-MS (ESI-TOF): calcd for $C_{26}H_{43}NO_3SiNa$ [M+Na]⁺: 468.2904, found: 468.2890.

(5Z,12E,15S,17Z)-15-Hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-amide (6): To a stirred



solution of amide **50** (24 mg, 53 μ mol, 1.0 equiv) in MeCN (1 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 210 μ L, ca. 5.3 mmol, ca. 100 equiv) in MeCN (0.2 mL). After stirring for 30 min at

this temperature, the reaction mixture was quenched with brine (3 mL) and extracted with EtOAc (5 × 5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, MeOH:CH₂Cl₂, 6:94) gave pure title compound (**6**, 12 mg, 36 µmol, 68 % yield) as a colorless oil. **6**: R_f=0.20 (EtOAc); $[\alpha]_D^{25}$ = +128.6 (*c* = 0.50 in C₆H₆); IR (film): v_{max} = 3347, 3211, 3009, 2965, 2936, 2844, 1738, 1648, 1578, 1458, 1405, 1345, 1210, 1054, 1033, 1012, 807, 692 cm⁻¹; ¹H-NMR (600 MHz, C₆D₆) δ 7.00 (dd, *J*=6.0, 2.6 Hz, 1 H), 6.85 (t, *J*=7.6 Hz, 1 H), 6.20 (dd, *J*=6.0, 1.8 Hz, 1 H), 6.06 (s, 1 H), 5.56 – 5.49 (m, 2 H), 5.38 – 5.31 (m, 1 H), 5.24 – 5.19 (m, 1 H), 3.85 (s, 1 H), 3.77 (quint, *J*=6.3 Hz, 1 H), 3.17 (ddt, *J*=8.8, 4.3, 2.0 Hz, 1 H), 2.53 – 2.46 (m, 2 H), 2.36 – 2.26 (m, 3 H), 2.12 – 2.06 (m, 1 H), 2.04 – 1.92 (m, 4 H), 1.91 – 1.83 (m, 2 H), 1.62 – 1.49 (m, 2 H), 1.29 (s, 1 H), 0.92 (t, *J*=7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 195.81, 175.60, 161.06, 139.58, 135.20, 134.28, 132.53, 131.95, 126.26, 125.27, 70.87, 43.75, 37.26, 35.35, 34.66, 30.52, 26.95, 25.41, 21.15, 14.49 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₉NO₃Na [M+Na]⁺: 354.2040, found: 354.2027.

(5Z,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-N-methyl-11-oxoprosta-5,9,12,17-

tetraen-1-amide (51): To a stirred solution of carboxylic acid 45¹ (30 mg, 67 µmol, 1.0 equiv) in



CH₂Cl₂ (1 mL) at 0 °C was added EDCI (26 mg, 0.13 mmol, 2.0 equiv) and 1-hydroxy benzotriazole (80 %, 25 mg, 0.13 mmol, 2.0 equiv). After stirring for 20 min at this temperature, methylamine (2.0 M in

THF, 67 μ L, 0.13 mmol, 2.0 equiv) was added. After stirring the resulting solution for an additional 2 h at 25 °C, the reaction mixture was then quenched with saturated aqueous NH₄Cl-solution (5 mL) and diluted with CH₂Cl₂ (15 mL). The phases were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 15 mL). The combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:3) gave pure title compound (**51**, 24 mg, 52 µmol, 78 % yield) as a colorless oil.

51: $R_f = 0.60$ (hexanes: EtOAc, 1:4); $[\alpha]_D^{25} = +115.3$ (c = 2.0 in CHCl₃); IR (film): $v_{max} = 3309$, 3010, 2955, 2930, 2857, 1702, 1651, 1543, 1462, 1361, 1253, 1085, 835, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.49 (dd, J = 5.8, 2.7 Hz, 1 H), 6.58 (t, J = 7.6 Hz, 1 H), 6.30 (dd, J = 6.0, 1.8 Hz, 1 H), 5.56 (br s, 1 H), 5.48 – 5.42 (m, 2 H), 5.37 – 5.31 (m, 2 H), 3.89 – 3.85 (m, 1 H), 3.45 – 3.44 (m, 1 H), 2.77 (d, J = 4.8 Hz, 3 H), 2.58 (dt, J = 14.4, 4.2 Hz, 1 H), 2.43 – 2.37 (m, 2 H), 2.27 – 2.11 (m, 5 H), 2.03 – 1.96 (m, 4 H), 1.66 (quint, J = 7.8 Hz, 2 H), 0.92 (t, J = 7.5 Hz, 3 H), 0.86 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.39, 173.32, 161.66, 138.84, 134.97, 134.11, 132.61, 131.71, 125.93, 124.32, 71.64, 43.41, 36.87, 36.00, 35.26, 30.56, 26.92, 26.36, 25.93, 25.51, 20.85, 18.16, 14.27, -4.46, -4.47 ppm; HR-MS (ESI-TOF): calcd for C₂₇H₄₆NO₃Si [M+H]⁺: 460.3241, found: 460.3258.

(5Z,12E,15S,17Z)-15-Hydroxy-N-methyl-11-oxoprosta-5,9,12,17-tetraen-1-amide (7): To a



stirred solution of *N*-methylamide **51** (24 mg, 52 μ mol, 1.0 equiv) in MeCN (1 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 210 μ L, ca. 5.2 mmol, ca. 100 equiv) in MeCN (0.5 mL). After stirring

for 30 min at this temperature, the reaction mixture was quenched with brine (3 mL) and extracted with CH_2Cl_2 (5 × 5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:9) gave pure title compound (**7**, 14 mg, 41 µmol, 78 % yield) as a colorless oil.

7: $R_f = 0.20$ (EtOAc); $[\alpha]_D^{25} = +153.6$ (c = 0.70 in CHCl₃); IR (film): $v_{max} = 3328$, 3009, 2935, 1697, 1649, 1562, 1411, 1208, 1047, 807, 717 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.52 (dd, J = 5.8, 2.7 Hz, 1 H), 6.61 (t, J = 7.6 Hz, 1 H), 6.34 (dd, J = 6.0, 1.7 Hz, 1 H), 5.60 – 5.55 (m, 1 H), 5.48 – 5.44 (m, 1 H), 5.42 – 5.37 (m, 1 H), 5.36 – 5.32 (m, 1 H), 3.86 – 3.82 (m, 1 H), 3.52 – 3.49 (m, 1 H), 2.79 (d, J = 4.9 Hz, 3 H), 2.67 – 2.63 (m, 1 H), 2.59 – 2.53 (m, 2 H), 2.49 – 2.45 (m, 1 H), 2.29 (t, J = 6.8 Hz, 2 H), 2.23 (dt, J = 15.6, 8.6 Hz, 1 H), 2.15 (t, J = 7.4 Hz, 2 H), 2.08 – 2.03 (m, 4 H), 1.71 – 1.63 (m, 3 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.53, 173.54, 161.78, 139.49, 135.49, 135.07, 131.97, 131.93, 125.78, 124.05, 70.72, 43.59, 36.86, 35.83, 34.91, 30.34, 26.97, 26.45, 25.47, 20.88, 14.32 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₃₁NO₃Na [M+Na]⁺: 368.2196, found: 368.2191.

(5Z,12E,15S,17Z)-15-{[*tert*-Butyl(dimethyl)silyl]oxy}-*N*-isopropyl-11-oxoprosta-5,9,12,17tetraen-1-amide (52): To a stirred solution of carboxylic acid 45¹ (30 mg, 0.067 mmol, 1.0 equiv)



in CH₂Cl₂ (1 mL) at 0 °C was added EDCI (25 mg, 0.13 mmol, 2.0 equiv) and 1-hydroxy benzotriazole (80 %, 25 mg, 0.13 mmol, 2.0 equiv). After stirring for 20 min at this temperature,

isopropylamine (11 μ L, 0.13 mmol, 2.0 equiv) was added. After stirring the resulting solution for an additional 6 h at 25 °C, the reaction mixture was then quenched with saturated aqueous NH₄Clsolution (5 mL) and diluted with CH₂Cl₂ (15 mL). The phases were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 15 mL). The combined organic extracts were washed with brine (5 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:4) gave pure title compound (**52**, 23 mg, 47 μ mol, 71 % yield) as a colorless oil.

52: $R_f = 0.60$ (hexanes: EtOAc, 1:4); $[\alpha]_D^{25} = +117.4$ (c = 2.0 in CHCl₃); IR (film): $v_{max} = 3301, 2958, 2930, 2858, 1702, 1646, 1543, 1461, 1252, 1063, 835 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) <math>\delta$ 7.48 (dd, J = 5.8, 2.7 Hz, 1 H), 6.59 (ddt, J = 8.3, 6.8, 1.2 Hz, 1 H), 6.31 (dd, J = 6.0, 1.8 Hz, 1 H), 5.48 – 5.44 (m, 2 H), 5.38 – 5.32 (m, 2 H), 5.26 (d, J = 6.1 Hz, 1 H), 4.10 – 4.02 (m, 1 H), 3.88 (quint, J = 5.9 Hz, 1 H), 3.45 (ddd, J = 8.6, 4.1, 2.1 Hz, 1 H), 2.59 (dt, J = 14.4, 4.2 Hz, 1 H), 2.46 – 2.37 (m, 2 H), 2.27 – 2.15 (m, 3 H), 2.09 (t, J = 6.6 Hz, 2 H), 2.02 – 1.97 (m, 3 H), 1.76 (s, 1 H), 1.66 (quint, J = 7.5 Hz, 2 H), 1.13 (d, J = 6.6 Hz, 6 H), 0.93 (t, J = 6.6 Hz, 3 H), 0.87 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.39, 171.76, 161.65, 138.85, 135.01, 134.13, 132.63, 131.77, 125.94, 124.37, 71.65, 43.42, 41.35, 36.88, 36.35, 35.28, 30.59, 26.91, 25.95, 25.89, 25.56, 22.94, 20.86, 18.18, 14.29, -4.45 ppm; HR-MS (ESI-TOF): calcd for C₂₉H₅₀NO₃Si [M+H]⁺: 488.3554, found: 488.3571.

(5Z,12E,15S,17Z)-15-Hydroxy-N-isopropyl-11-oxoprosta-5,9,12,17-tetraen-1-amide (8): To a



stirred solution of dienone *N-iso*-propylamide **52** (22 mg, 45 μ mol, 1.0 equiv) in MeCN (1 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 180 μ L, ca. 4.5 mmol, ca. 100 equiv) in MeCN (0.5 mL).

After stirring for 30 min at this temperature, the reaction mixture was quenched with brine (3 mL) and extracted with EtOAc (5 \times 5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column

chromatography (SiO₂, hexanes:EtOAc, 1:10) gave pure title compound (**8**, 12 mg, 34 µmol, 75 % yield) as a colorless oil.

8: $R_f = 0.30$ (EtOAc); $[\alpha]_D^{25} = +122.9$ (c = 1.2 in CHCl₃); IR (film): $v_{max} = 3301$, 2966, 2932, 1697, 1643, 1544, 1457, 1366, 1175, 1047, 809, 717 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.52 (dd, J = 5.9, 2.2 Hz, 1 H), 6.62 (t, J = 7.7 Hz, 1 H), 6.33 (dd, J = 6.0, 1.8 Hz, 1 H), 5.59 – 5.54 (m, 1 H), 5.49 – 5.44 (m, 1 H), 5.42 – 5.31 (m, 2 H), 4.09 – 4.01 (m, 1 H), 3.86 – 3.81 (m, 1 H), 3.51 – 3.49 (m, 1 H), 2.65 (dt, J = 14.8, 5.7 Hz, 1 H), 2.61 (d, J = 3.7 Hz, 1 H), 2.57 – 2.52 (m, 1 H), 2.49 – 2.45 (m, 1 H), 2.28 (t, J = 7.0 Hz, 2 H), 2.22 (dt, J = 15.7, 8.3 Hz, 1 H), 2.11 (t, J = 7.3 Hz, 2 H), 2.07 – 2.02 (m, 4 H), 1.76 (brs, 1 H), 1.71 – 1.62 (m, 2 H), 1.12 (d, J = 6.7 Hz, 6 H), 0.95 (t, J = 7.6 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.50, 171.94, 161.77, 139.43, 135.43, 135.06, 131.98, 131.92, 125.74, 124.07, 70.69, 43.59, 41.42, 36.83, 36.18, 34.89, 30.34, 26.95, 25.55, 22.92, 20.87, 14.31 ppm; HR-MS (ESI-TOF): calcd for C₂₃H₃₆NO₃ [M+H]⁺: 374.2690, found: 374.2694.

(5Z,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-N,N-dimethyl-11-oxoprosta-5,9,12,17-

tetraen-1-amide (53): To a stirred solution of carboxylic acid 45¹ (12 mg, 30 µmol, 1.0 equiv) in



CH₂Cl₂ (1 mL) at 0 °C was added EDCI (8.0 mg, 45 μ mol, 1.5 equiv) and 1-hydroxy benzotriazole (80 %, 8.0 mg, 45 μ mol, 1.5 equiv). After stirring at this temperature for 20 min, dimethyl amine (2.0 M in THF,

16 μ L, 32 μ mol, 1.2 equiv) was added. After stirring the resulting solution for an additional 3 h at 25 °C, the reaction mixture was quenched with saturated aqueous NH₄Cl-solution (75 mL) and diluted with CH₂Cl₂ (15 mL). The phases were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 15 mL). The combined organic extracts were washed with brine (5 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:4) gave pure title compound (**53**, 8.8 mg, 21 µmol, 71 % yield) as a colorless oil.

53: $R_f = 0.60$ (EtOAc); $[\alpha]_D^{25} = +123.3$ (c = 0.60 in C_6H_6); IR (film): $v_{max} = 3009$, 2955, 2929, 2856, 1703, 1653, 1462, 1397, 1256, 1083, 836, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.49 (dd, J = 5.8, 2.7 Hz, 1 H), 6.60 (t, J = 7.6 Hz, 1 H), 6.31 (dd, J = 6.0, 1.8 Hz, 1 H), 5.55 – 5.45 (m, 2 H), 5.38 – 5.33 (m, 2 H), 3.88 (quint, J = 6.2 Hz, 1 H), 3.47 – 3.44 (m, 1 H), 2.98 (s, 3 H), 2.93 (s, 3 H), 2.62 (dt, J = 14.4, 5.7 Hz, 1 H), 2.47 – 2.38 (m, 2 H), 2.28 (t, J = 7.5 Hz, 2 H), 2.25 – 2.15 (m, 3 H),

2.10 – 1.97 (m, 4 H), 1.68 (quint, J=7.5 Hz, 2 H), 0.93 (t, J=7.5 Hz, 3 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.41, 172.78, 161.70, 138.87, 135.00, 134.13, 132.61, 132.05, 125.85, 124.41, 71.68, 43.48, 37.33, 36.91, 35.50, 35.30, 32.78, 30.65, 27.12, 25.97, 24.99, 20.88, 18.20, 14.31, -4.43 ppm; HR-MS (ESI-TOF): calcd for C₂₈H₄₇NO₃SiNa [M+Na]⁺: 496.3217, found: 496.3201.

(5*Z*,12*E*,15*S*,17*Z*)-15-Hydroxy-*N*,*N*-dimethyl-11-oxoprosta-5,9,12,17-tetraen-1-amide (9):

To a stirred solution of dienone N,N-dimethylamide 53 (6.0 mg, 13 µmol, 1.0 equiv) in MeCN

(1 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 46 µL, ca. 1.3 mmol, ca. 100 equiv) in MeCN (0.5 mL). After stirring for 30 min at this temperature, the reaction mixture was quenched with

brine (3 mL) and extracted with CH_2Cl_2 (5 × 5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:10) gave pure title compound (**9**, 3.8 mg, 11 µmol, 84 % yield) as a colorless oil.

9: $R_f = 0.30$ (EtOAc); $[\alpha]_D^{25} = +116.0$ (c = 0.3 in CHCl₃); IR (film): $v_{max} = 3419$, 3409, 3008, 2959, 2927, 2872, 1697, 1626, 1579, 1400, 1260, 1048, 801 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.53 (dd, J = 5.8, 2.7 Hz, 1 H), 6.62 (t, J = 7.6 Hz, 1 H), 6.34 (dd, J = 6.0, 1.8 Hz, 1 H), 5.59 – 5.54 (m, 1 H), 5.52 – 5.47 (m, 1 H), 5.43 – 5.33 (m, 2 H), 3.86 – 3.81 (m, 1 H), 3.52 – 3.49 (m, 1 H), 2.99 (s, 3 H), 2.93 (s, 3 H), 2.71 – 2.67 (m, 2 H), 2.58 (dt, J = 14.6, 7.1 Hz, 1 H), 2.48 (ddd, J = 14.6, 8.2, 6.5 Hz, 1 H), 2.31 – 2.28 (m, 4 H), 2.21 (dt, J = 15.8, 8.8 Hz, 1 H), 2.11 – 2.03 (m, 4 H), 1.71 – 1.64 (m, 2 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.50, 172.91, 161.75, 139.47, 135.35, 135.07, 132.22, 131.97, 125.68, 124.19, 70.71, 43.72, 37.40, 36.95, 35.64, 34.86, 32.61, 30.43, 27.20, 24.95, 20.89, 14.34 ppm; HR-MS (ESI-TOF): calcd for C₂₂H₃₃NO₃Na [M+Na]⁺: 382.2353, found: 382.2365.

Synthesis of Δ^{12} -PGJ₃ Analog 12:

To a stirred solution of dienone 54^1 (18.0 mg, 32.6 µmol, 1.0 equiv) in MeCN (0.3 mL) at -10 °C was dropwise added a solution of HF (50% aq., 67 µL, ca. 1.63 mmol, ca. 50 equiv) in MeCN (0.3 mL). After stirring for 2 h at this temperature, the reaction mixture was quenched with sat. aq. NaHCO₃-solution (5 mL), and extracted with EtOAc (3×5 mL). The combined organic extracts were washed with sat. brine (3 mL), dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 0.1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 2:1) yielded pure title compound (**55**, 12.4 mg, 28.4 µmol, 87 % yield) as a colorless oil.

55: $R_f = 0.51$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{25} = +142.5$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 3430$, 3007, 2931, 2856, 1700, 1651, 1612, 1583, 1513, 1461, 1246, 1173, 1097, 1036 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ 7.50 (ddd, J = 6.1, 2.6, 1.0 Hz, 1 H), 7.25 (d, J = 8.8 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.63 (tt, J = 7.0, 1.4 Hz, 1 H), 6.33 (dd, J = 6.0, 1.8 Hz, 1 H), 5.63 – 5.54 (m, 1 H), 5.51 – 5.44 (m, 1 H), 5.41 – 5.27 (m, 2 H), 4.42 (s, 2 H), 3.80 (s, 3 H), 3.48 (dq, J = 6.6, 2.1 Hz, 1 H), 3.42 (t, J = 6.5 Hz, 2 H), 2.60 (dddd, J = 12.5, 6.4, 4.5, 2.1 Hz, 1 H), 2.54 – 2.41 (m, 2 H), 2.31 – 2.17 (m, 3 H), 2.10 – 1.92 (m, 6 H), 1.62 – 1.54 (m, 2 H), 1.40 (dq, J = 10.1, 7.5 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (125 MHz, CDCl₃) δ 196.53, 161.98, 159.22, 139.55, 135.85, 134.94, 132.72, 131.68, 130.73, 129.37, 125.05, 123.84, 113.86, 72.67, 70.57, 69.97, 55.40, 43.48, 36.58, 35.03, 30.43, 29.50, 27.30, 26.28, 20.89, 14.36 ppm; HR-MS (ESI-TOF): calcd for C₂₈H₃₈O₄Na [M+Na]⁺: 461.2662, found: 461.2647.

(5Z,12E,15S,17Z)-1,15-Dihydroxyprosta-5,9,12,17-tetraen-11-one (12): To a vigorously stirred solution of Δ^{12} -PGJ₃ para-methoxybenzylether 55 (9.0 mg, 21 µmol, 1.0 equiv) in a mixture of CH₂Cl₂:H₂O (4:1, 0.5 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (7.0 mg, 31 µmol, 1.5 equiv). After stirring at this temperature for 60 min, the reaction mixture was diluted with Et₂O (5 mL), filtered through Celite, washed with Et₂O, and concentrated to a volume of ca. 0.1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 1:1→0:1) yielded pure title compound (12, 6.0 mg, 19 µmol, 92 % yield) as a colorless oil.

12: $R_f = 0.21$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{25} = +151.2$ (c = 0.6 in C_6H_6); IR (film): $v_{max} = 3385$, 3009, 2928, 2857, 1695, 1648, 1579, 1456, 1210, 1048 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ 7.52 (ddd, J = 6.0, 2.6, 1.0 Hz, 1 H), 6.63 (ddt, J = 8.3, 7.0, 1.3 Hz, 1 H), 6.34 (dd, J = 6.0, 1.8 Hz, 1 H), 5.60 (dtt, J = 10.5, 7.3, 1.5 Hz, 1 H), 5.53 – 5.44 (m, 1 H), 5.40 – 5.29 (m, 2 H), 3.84 (quint, J = 6.3 Hz, 1 H), 3.63 (t, J = 6.5 Hz, 2 H), 3.54 – 3.47 (m, 1 H), 2.63 (dddd, J = 13.0, 6.4, 4.3, 2.2 Hz, 1 H), 2.58 – 2.42 (m, 2 H), 2.31 – 2.19 (m, 3 H), 2.04 (dddd, J = 17.6, 8.3, 7.3, 1.6 Hz, 4 H), 1.60 – 1.51

(m, 2 H), 1.46 - 1.37 (m, 2 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (125 MHz, CDCl₃) δ 196.59, 161.97, 139.61, 135.93, 135.01, 132.67, 131.72, 125.15, 123.81, 70.65, 62.76, 43.53, 36.62, 35.01, 32.36, 30.45, 27.21, 25.80, 20.90, 14.37 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₃₀O₃Na [M+Na]⁺: 341.2087, found: 341.2078.

Synthesis of Δ^{12} -PGJ₃ Analogs *ent*-1, *ent*-2, and *ent*-11:

(4S)-4-{(2Z)-7-[(4-Methoxybenzyl)oxy]hept-2-en-1-yl}cyclopent-2-en-1-one (ent-57): To a stirred

OPMB ent-57 solution of PMB ether **56** (460 mg, 0.980 mmol, 1.0 equiv) in Et₂O (5 mL) at -10 °C was dropwise added diisobutylaluminum hydride (1.0 M in CH₂Cl₂, 1.47 mL, 1.47 mmol, 1.5 equiv). After stirring for

30 min, the clear solution was cooled to -78 °C and quenched with MeOH (2 mL), diluted with Et₂O (50 mL) and allowed to warm to 25 °C. Under vigorous stirring, saturated Na-K tartrate-solution (50 mL) was added and the resulting mixture was stirred for an additional 3 h. The resultant biphasic mixture was extracted with Et₂O (3 × 50 mL), and the combined organic layers were washed sequentially with aq. HCl (1 M, 2 × 10 mL), H₂O (30 mL) and brine (30 mL). The organic phase was dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 19:1→4:1) gave pure title compound (*ent*-**57**, 230 mg, 0.744 mmol, 76% yield) as a colorless oil.

ent-**57**: $R_f = 0.57$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = -88.5$ (c = 1.0 in C_6H_6); lit.: $[\alpha]_D^{25} = +90.5$ (c = 1.0 in C_6H_6) for the other enantiomer. All other analytical data were identical to those reported in the literature.¹

(5Z,8β,12E,15R,17Z)-15-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-[(4-methoxybenzyl)oxy]prosta-5,9,12,17-tetraen-11-one (*ent*-54): To a stirred solution of diisopropylamine (318 μL, 2.27 mmol,



2.1 equiv) in THF (12 mL) at 0 °C was dropwise added, *n*-butyl lithium (1.6 M in hexanes, 1.35 mL, 2.16 mmol, 2.0 equiv). After stirring for 20 min at this temperature, the clear solution was cooled

to -78 °C and a solution of enone *ent*-**57** (340 mg, 1.08 mmol, 1.0 equiv) in THF (8 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 20 min at this temperature, a solution of aldehyde *ent*-**58** (331 mg, 1.30 mmol, 1.2 equiv) in THF (8 mL) was added dropwise and stirring at this temperature was continued for an additional 30 min. The

reaction mixture was then quenched with sat. aqueous NH₄Cl-solution (15 mL), diluted with EtOAc (75 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with EtOAc (2×75 mL), and the combined organic extracts were washed with sat. brine (50 mL), dried (Na₂SO₄), filtered, and concentrated. The crude aldol product **59** was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereoisomers as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of above aldol product **59** in CH₂Cl₂ (12 mL) at 0 °C was added DMAP (1.32 g, 10.8 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (168 µL, 2.16 mmol, 2.0 equiv). After stirring for 30 min at this temperature, the reaction mixture was allowed to warm to 25 °C and stirred for 6 h. The reaction mixture was quenched with saturated aqueous NaHCO₃-solution (10 mL) and diluted with CH₂Cl₂ (50 mL). The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 50 mL), and the combined organic extracts were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 7:1) gave pure title compound (*ent*-**54**, 219 mg, 0.531 mmol, 49 % yield for two steps) as a colorless oil. *ent*-**54**: R_f=0.70 (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = -124.1$ (*c* = 1.0 in C₆H₆); lit.: $[\alpha]_D^{25} = +125.0$ (*c* = 1.0 in C₆H₆) for the other enantiomer. All other analytical data were identical to those reported for its

in C_6H_6) for the other enantiomer. All other analytical data were identical to those reported for : enantiomer.¹

(5Z,8β,12E,15S,17Z)-15-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-hydroxyprosta-5,9,12,17-tetraen-

11-one (60): To a vigorously stirred solution of dienone *ent*-**54** (125 mg, 0.230 mmol, 1.0 equiv) in a mixture of CH₂Cl₂:H₂O (16:1, 6 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (78.2 mg, 0.345 mmol, 1.5 equiv). After stirring at this temperature for 45 min, the reaction mixture was diluted with Et₂O (30 mL), filtered through Celite, washed with Et₂O, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 2:1) yielded pure title compound (**60**, 85.6 mg, 0.200 mmol, 87 % yield) as a colorless oil.

60: $R_f = 0.38$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = -140.7$ (c = 1.0 in C_6H_6); lit.: $[\alpha]_D^{25} = +146.7$ (c = 1.0 in C_6H_6) for the other enantiomer. All other analytical data were identical to those reported in the literature.¹

(5Z,8β,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-11-oxoprosta-5,9,12,17-tetraen-1-

oic acid (ent-45): To a vigorously stirred solution of hydroxy dienone 60 (96 mg, 0.22 mmol,



pyridinium chlorochromate (95 mg, 0.44 mmol, 2.0 equiv). After stirring for 2 h, the reaction mixture was diluted with Et₂O (30 mL),

filtered through Celite, washed with Et₂O, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 5:1) yielded aldehyde 61, which was directly carried to next step without further characterization.

To a vigorously stirred solution of above aldehyde dienone **61** in *t*-BuOH (4 mL) at 25 °C were sequentially dropwise added 2-methyl-2-butene (470 µL, 4.2 mmol, 20 equiv), a solution of NaH₂PO₄ (98 mg, 0.63 mmol, 3.0 equiv) in H₂O (1.5 mL) and a solution of NaClO₂ (80%, 71 mg, 0.63 µmol, 3.0 equiv) in H₂O (1.5 mL). After stirring for 30 min, the reaction mixture was diluted with a solution of NaH₂PO₄ (4.0 g) in H₂O (80 mL) and extracted with EtOAc (5×80 mL). The combined organic extracts were washed with sat. brine (50 mL), dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, CH₂Cl₂:EtOH, 20:1) yielded pure title compound (*ent*-45, 84 mg, 0.19 mmol, 86% for two steps) as a colorless oil.

ent-45: $R_f = 0.57$ (CH₂Cl₂:EtOH, 10:1); $[\alpha]_D^{25} = -143.8$ (c = 0.5 in C₆H₆); lit.: $[\alpha]_D^{25} = +140.5$ (c = 1.0in C_6H_6) for the other enantiomer. All other analytical data were identical to those reported in the literature.¹

(5Z,8β,12E,15R,17Z)-15-Hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oic acid (ent-1): To a stirred solution of $ent-\Delta^{12}$ -PGJ₃-15-*t*-butyldimethylsilyl-ether (*ent*-45) соон (80 mg, 0.18 mmol, 1.0 equiv) in MeCN (1.5 mL) at 0 °C was dropwise δн added a solution of HF (50 % aq., 720 µL, ca. 18 mmol, ca. 100 equiv) ent-1

in MeCN (0.5 mL). After stirring for 45 min at this temperature, the reaction mixture was quenched with sat. brine (30 mL) and extracted with EtOAc (5 \times 50 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, CH₂Cl₂:EtOH, 15:1) yielded the pure title compound (ent-1, 53 mg, 0.16 mmol, 92 % yield) as a colorless oil.

ent-1: $R_f = 0.56$ (CH₂Cl₂:EtOH, 10:1), $[\alpha]_D^{25} = -128.2$ (c = 1.0 in C_6H_6), lit.: $[\alpha]_D^{25} = +129.0$ (c = 0.5 in C_6H_6) for the other enantiomer. All other analytical data were identical to those reported in the literature.¹

Methyl (5Z,8β,12E,15R,17Z)-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oate (ent-2): To a



stirred solution of *ent*- Δ^{12} -PGJ₃ (*ent*-1) (10 mg, 30 µmol, 1.0 equiv) in C₆H₆:MeOH (3:2, 1.0 mL) at 25 °C was dropwise added a solution of trimethylsilyl diazomethane (2 M in Et₂O, 23 µL,

45 µmol, 1.5 equiv) (yellow color persists). After stirring for 30 min, the reaction mixture was concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 2:1 \rightarrow 3:2) yielded pure title compound (*ent*-2, 9.0 mg, 28 µmol, 93 % yield) as a colorless oil.

*ent-***2:** $R_f = 0.53$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{25} = +194.3$ (c = 0.9 in C_6H_6); lit.: $[\alpha]_D^{25} = +206.3$ (c = 0.4 in C_6H_6) for the other enantiomer. All other analytical data were identical to those of the enantiomer reported in the literature.²

(5Z,8β,12E,15R,17Z)-1,15-Epoxyprosta-5,9,12,17-tetraene-1,11-dione (ent-11): To a stirred



solution of 2-methyl-6-nitrobenzoic anhydride (15 mg, 42 µmol, 1.4 equiv) and 4-dimethylaminopyridine (22 mg, 180 µmol, 6.0 equiv) in CH₂Cl₂ (20 mL) was added a solution of *ent*- Δ^{12} -PGJ₃ (*ent*-1) (10 mg, 30 µmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at 25 °C dropwise via syringe pump over 15 h.

After stirring for an additional 2 h, the reaction mixture was washed sequentially with sat. aq. NaHCO₃-solution (10 mL), aq. HCl (0.2 M, 10 mL), and sat. brine (10 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, hexanes: EtOAc, 3:1) yielded pure title compound (*ent*-**11**, 7.1 mg, 22 µmol, 74 % yield) as a white solid. *ent*-**11:** $R_f = 0.35$ (hexanes:EtOAc, 3:1); mp = 62-65 °C; $[\alpha]_D^{25} = -64.0$ (c = 0.7 in CHCl₃); lit.:

 $[\alpha]_D^{25} = +65.2$ (*c* = 0.6 in C₆H₆) for the other enantiomer. All other analytical data were identical to those of the enantiomer reported in the literature.²

Synthesis of 15-Deoxy- $\Delta^{12,14}$ -PGJ₃ (13) and its Methyl Ester (14):

(4*R*)-4-[(2*Z*)-7-Hydroxyhept-2-en-1-yl]cyclopent-2-en-1-one (62): To a vigorously stirred solution of enone 57 (500 mg, 1.59 mmol, 1.0 equiv) in a mixture of CH₂Cl₂:H₂O (20:1, 8 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (540 mg, 2.40 mmol, 1.5 equiv). After stirring at this temperature for 2 h, the reaction mixture was diluted with EtOAc (30 mL), filtered through Celite, washed with EtOAc (50 mL), and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, $10:1\rightarrow2:1$) gave pure title compound (62, 291 mg, 1.49 mmol, 94 % yield) as a colorless oil.

62: $R_f = 0.38$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = +80.1$ (c = 0.47 in CHCl₃); IR (film): $v_{max} = 3421$, 3008, 2931, 2860, 1706, 1670, 1585, 1184, 1056, 785 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.62 (dd, J = 5.8, 2.7 Hz, 1 H), 6.17 (dd, J = 5.9, 2.0 Hz, 1 H), 5.53 – 5.49 (m, 1 H), 5.39 – 5.34 (m, 1 H), 3.64 (t, J = 6.5 Hz, 3 H), 3.03 – 2.98 (m, 1 H), 2.51 (dd, J = 19.7, 6.5 Hz, 1 H), 2.33 – 2.28 (m, 1 H), 2.24 – 2.19 (m, 1 H), 2.08 – 2.00 (m, 3 H), 1.60 – 1.55 (m, 2 H), 1.46 – 1.41 (m, 2 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 210.00, 168.06, 134.25, 132.46, 126.00, 62.88, 41.51, 40.62, 32.43, 32.09, 27.19, 25.82 ppm; HR-MS (ESI-TOF): calcd for C₁₂H₁₉O₂ [M+H]⁺: 195.1386, found: 195.1377.

(4R)-4-[(2Z)-7-{[tert-Butyl(dimethyl)silyl]oxy}hept-2-en-1-yl]cyclopent-2-en-1-one (63): To a

stirred solution of hydroxy enone **62** (220 mg, 1.10 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) at 25 °C were added sequentially imidazole (440 mg, 3.30 mmol, 3.0 equiv) and TBSCl (280 mg, 1.65 mmol, 1.5 equiv). The reaction mixture was stirred for 4 h at the same temperature, quenched with saturated aqueous NH₄Cl-solution (3 mL), the phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were washed with H₂O (10 mL), dried (MgSO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 8:1) gave pure title compound (**63**, 300 mg, 0.981 mmol, 89 % yield) as a colorless oil.

63: $R_f = 0.40$ (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = +93.3$ (c = 1.00 in C_6H_6); IR (film): $v_{max} = 3008$, 2929, 2857, 1716, 1587, 1472, 1408, 1254, 1180, 1099, 1006, 835, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.62 (dd, J = 5.8, 2.7 Hz, 1 H), 6.16 (dd, J = 5.9, 2.0 Hz, 1 H), 5.53 – 5.48 (m, 1 H), 5.37

- 5.33 (m, 1 H), 3.59 (td, J = 6.5, 1.3 Hz, 2 H), 3.01 – 2.98 (m, 1 H), 2.51 (dd, J = 18.8, 6.5 Hz, 1 H), 2.32 – 2.27 (m, 1 H), 2.24 – 2.19 (m, 1 H), 2.05 – 1.99 (m, 3 H), 1.53 – 1.48 (m, 2 H), 1.42 – 1.36 (m, 2 H), 0.88 (s, 9 H), 0.03 (s, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 209.97, 168.08, 134.23, 132.77, 125.74, 63.11, 41.55, 40.64, 32.58, 32.08, 27.26, 26.09, 25.77, 18.47, –5.15 ppm; HR-MS (ESI-TOF): calcd for C₁₈H₃₃O₂Si [M+H]⁺: 309.2251, found: 309.2234.

(5Z,12E,14E,17Z)-1-{[*tert*-Butyl(dimethyl)silyl]oxy}prosta-5,9,12,14,17-pentaen-11-one (66):



To a stirred solution of diisopropylamine (230 μ L, 1.64 mmol, 2.05 equiv) in THF (12 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M in hexanes, 640 μ L, 1.60 mmol, 2.0 equiv). After stirring for 20 min at this

temperature, the clear solution was cooled to -78 °C and a solution of enone 63 (240 mg, 0.802 mmol, 1.0 equiv) in THF (8 mL) was added dropwise. After stirring for an additional 20 min at this temperature, a solution of aldehyde² 64 (147 mg, 1.20 mmol, 1.5 equiv) in THF (8 mL) was added dropwise and stirring at this temperature was continued for an additional 30 min. The reaction mixture was then quenched by addition of saturated aqueous NH₄Cl-solution (75 mL), diluted with EtOAc (75 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with EtOAc (2×75 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereoisomers (65, 274 mg, 0.630 mmol, 79% yield) as a colorless oil, which was taken to the next step without further purification. To a stirred solution of the aldol product 65 (274 mg, 0.630 mmol, 1.0 equiv) in CH₂Cl₂ (6 mL) at -10 °C was added DMAP (770 mg, 6.30 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (100 µL, 1.26 mmol, 2.0 equiv). After stirring for 30 min at this temperature, the reaction mixture was allowed to warm to 25 °C and stirred for 6 h. The reaction mixture was quenched with saturated aqueous NaHCO₃-solution (10 mL), diluted with CH₂Cl₂ (50 mL), the phases were separated, the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic extracts were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes: EtOAc, 7:1) gave pure title compound (66, 102 mg, 0.246 mmol, 31 % yield for the two steps) as a colorless oil.

66: $R_f = 0.70$ (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = +58.1$ (c = 0.90 in C₆H₆); IR (film): $v_{max} = 2941$, 2865, 1697, 1633, 1462, 1207, 1104, 1067, 882 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.48 (dd, J = 6.0, 2.4 Hz, 1 H), 6.96 (d, J = 11.8 Hz, 1 H), 6.37 – 6.33 (m, 2 H), 6.21 (dt, J = 13.1, 6.1 Hz, 1 H), 5.56 – 5.47 (m, 2 H), 5.40 – 5.31 (m, 2 H), 3.60 – 3.55 (m, 3 H), 2.97 (t, J = 6.9 Hz, 2 H), 2.63 – 2.58 (m, 1 H), 2.27 (dt, J = 15.3, 8.7 Hz, 1 H), 2.09 – 2.04 (m, 2 H), 2.02 – 1.90 (m, 2 H), 1.52 – 1.55 (m, 2 H), 1.40 – 1.34 (m, 2 H), 0.98 (t, J = 7.8 Hz, 3 H), 0.89 (s, 9 H), 0.04 (s, 3 H), 0.04 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 197.48, 160.95, 144.24, 135.68, 135.36, 134.10, 132.90, 131.42, 125.84, 125.07, 124.60, 63.15, 43.77, 32.65, 31.14, 30.99, 27.28, 26.08, 25.99, 20.70, 18.44, 14.32, -5.22 ppm; HR-MS (ESI-TOF): calcd for C₂₆H₄₃O₂Si [M+H]⁺: 415.3027, found: 415.3021.

(5Z,12E,14E,17Z)-1-Hydroxyprosta-5,9,12,14,17-pentaen-11-one (67): To a stirred solution of trienone 66 (95 mg, 0.23 mmol, 1.0 equiv) in MeCN (3.5 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 460 μ L, ca. 12 mmol, ca. 50 equiv) in MeCN (3.5 mL). After stirring for 10 min at this temperature,

the reaction mixture was quenched with brine (30 mL) and extracted with EtOAc (5×50 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:3) gave pure title compound (**67**, 61 mg, 0.20 mmol, 87 % yield) as a colorless oil.

67: $R_f = 0.30$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = +134.2$ (c = 0.40 in C_6H_6); IR (film): $v_{max} = 3423$, 3009, 2930, 2859, 1686, 1626, 1578, 1456, 1298, 1206, 1067, 976, 818, 725, 519 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.48 (dd, J = 6.0, 2.4 Hz, 1 H), 6.96 (d, J = 11.8 Hz, 1 H), 6.37 – 6.33 (m, 2 H), 6.22 (dt, J = 13.5, 6.7 Hz, 1 H), 5.55 – 5.46 (m, 2 H), 5.40 – 5.32 (m, 2 H), 3.63 (t, J = 6.5 Hz, 3 H), 3.57 (m, 1 H), 2.98 (t, J = 6.7 Hz, 2 H), 2.60 (dt, J = 12.4, 5.9 Hz, 1 H), 2.29 (dt, J = 15.1, 9.0 Hz, 1 H), 2.09 – 2.04 (m, 4 H), 1.57 – 1.53 (m, 2 H), 1.43 – 1.38 (m, 2 H), 0.98 (t, J = 7.8 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 197.49, 160.88, 144.32, 135.68, 135.42, 134.12, 132.62, 131.46, 125.81, 125.27, 124.60, 62.93, 43.70, 32.47, 31.15, 30.94, 27.19, 25.84, 20.71, 14.32 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₈O₂Na [M+Na]⁺: 323.1986, found: 323.1976.

(5Z,12E,14E,17Z)-11-Oxoprosta-5,9,12,14,17-pentaen-1-oic acid (13): To a vigorously stirred



solution of hydroxy trienone **67** (20 mg, 66 μ mol, 1.0 equiv) in CH₂Cl₂ (2 mL) at 25 °C was added in one portion pyridinium chlorochromate (30 mg, 130 μ mol, 2.0 equiv). After stirring for 2 h, the reaction mixture

was directly, and without any further work-up, loaded onto a column. Flash column chromatography (SiO₂, hexanes:EtOAc, $7:1\rightarrow5:1$) gave the intermediate aldehyde, which was immediately used in the next reaction. To a vigorously stirred solution of the aldehyde in *t*-BuOH (1.5 mL) at 25 °C were sequentially added 2-methyl-2-butene (46 µL, 0.66 mmol, 10 equiv), a solution of NaH₂PO₄ (0.30 M in H₂O, 0.33 mL, 0.10 mmol, 1.5 equiv) and a solution of NaClO₂ (80% purity, 11 mg, 0.10 mmol, 1.5 equiv) in H₂O (0.5 mL). After stirring for 30 min, the reaction mixture was diluted with a solution of NaH₂PO₄ (0.30 M, 4 mL) and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:9) gave pure title compound (**13**, 14 mg, 44 µmol, 67 % yield for the two steps) as a colorless oil.

13: $R_f = 0.60$ (EtOAc); $[\alpha]_D^{25} = +134.2$ (c = 0.40 in C_6H_6); IR (film): $v_{max} = 3015$, 2962, 2932, 1706, 1624, 1406, 1211, 997, 526 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.47 (dd, J = 6.0, 2.4 Hz, 1 H), 6.96 (d, J = 11.8 Hz, 1 H), 6.37 – 6.32 (m, 2 H), 6.22 (dt, J = 13.5, 6.7 Hz, 1 H), 5.56 – 5.51 (m, 1 H), 5.48 – 5.43 (m, 1 H), 5.40 – 5.35 (m, 2 H), 3.60 – 3.57 (m, 1 H), 2.97 (t, J = 6.7 Hz, 2 H), 2.59 (dt, J = 14.8, 5.8 Hz, 1 H), 2.34 – 2.27 (m, 3 H), 2.09 – 2.03 (m, 4 H), 1.68 (quint, J = 7.5 Hz, 2 H), 0.98 (t, J = 7.6 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 197.52, 178.35, 160.83, 144.49, 135.53, 135.49, 134.13, 131.60, 131.48, 126.16, 125.76, 124.58, 43.58, 33.26, 31.14, 30.84, 26.68, 24.55, 20.70, 14.31 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₆O₃Na [M+Na]⁺: 337.1774, found: 337.1769.



(yellow color persists). After stirring for 30 min, the reaction mixture was concentrated under

reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, $2:1\rightarrow 3:2$) gave pure title compound (**14**, 3.6 mg, 12 µmol, 90 % yield) as a colorless oil.

14: $R_f = 0.53$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{25} + 189.2$ (c = 0.70 in C_6H_6); IR (film): $v_{max} = 3010, 2932, 1736, 1693, 1631, 1579, 1436, 1365, 1205, 983, 837, 728 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) <math>\delta$ 7.47 (dd, J = 6.0, 2.4 Hz, 1 H), 6.96 (d, J = 11.8 Hz, 1 H), 6.37 – 6.32 (m, 2 H), 6.21 (dt, J = 13.5, 6.7 Hz, 1 H), 5.56 – 5.51 (m, 1 H), 5.48 – 5.43 (m, 1 H), 5.40 – 5.35 (m, 2 H), 3.66 (s, 3 H), 3.59 – 3.56 (m, 1 H), 2.97 (t, J = 6.7 Hz, 2 H), 2.59 (dt, J = 14.8, 5.8 Hz, 1 H), 2.30 – 2.25 (m, 3 H), 2.09 – 2.01 (m, 4 H), 1.67 (quint, J = 7.5 Hz, 2 H), 0.98 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 197.42, 174.01, 160.78, 144.40, 135.57, 135.47, 134.10, 131.63, 131.49, 126.03, 125.78, 124.59, 51.63, 43.62, 33.52, 31.14, 30.87, 26.79, 24.82, 20.70, 14.31 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₂₈O₃Na [M+Na]⁺: 351.1931, found: 351.1923.

Synthesis of 15-Deoxy- Δ^{12} -PGJ₃ (15) and its Methyl Ester (16):

(5Z,12E,17Z)-1-[(4-Methoxybenzyl)oxy]prosta-5,9,12,17-tetraen-11-one (71): To a stirred



solution of diisopropylamine (74 μ L, 0.52 mmol, 2.1 equiv) in THF (3 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M in hexanes, 0.20 mL, 0.50 mmol, 2.0 equiv). After stirring for 20 min at this

temperature, the clear solution was cooled to -78 °C and a solution of enone **57** (80 mg, 0.25 mmol, 1.0 equiv) in THF (2 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 15 min at this temperature, a solution of aldehyde **56**³ (50 mg, 0.38 mmol, 1.5 equiv) in THF (1 mL) was added dropwise and stirring at this temperature was continued for an additional 30 min. The reaction mixture was then quenched with saturated aqueous NH₄Cl-solution (5 mL), diluted with EtOAc (30 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with EtOAc (2 × 10 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereoisomers (**70**, 98 mg, 0.22 mmol, 88 % yield) as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of the aldol product **70** (98 mg, 0.22 mmol) in CH_2Cl_2 (4 mL) at 25 °C was added DMAP (270 mg, 2.2 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (34 μ L, 0.44 mmol, 2.0 equiv). After stirring for 6 h at this temperature, the reaction

mixture was quenched with saturated NaHCO₃-solution (5 mL) and diluted with CH₂Cl₂ (20 mL). The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2×10 mL), and the combined organic extracts were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 7:1) gave pure title compound (**71**, 66 mg, 0.15 mmol, 61 % yield for the two steps) as a colorless oil.

71: $R_f = 0.60$ (hexanes: EtOAc, 3:1); $[\alpha]_D^{25} = +136.3$ (c = 1.00 in C_6H_6); IR (film): $v_{max} = 3005$, 2933, 2858, 1702, 1654, 1613, 1583, 1513, 1458, 1301, 1247, 1172, 1099, 1036, 820 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.47 (dd, J = 6.0, 2.4 Hz, 1 H), 7.25 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.57 (t, J = 7.5 Hz, 1 H), 6.32 (dd, J = 6.0, 1.7 Hz, 1 H), 5.50 – 5.45 (m, 1 H), 5.43 – 5.38 (m, 1 H), 5.34 – 5.28 (m, 2 H), 4.42 (s, 2 H), 3.80 (s, 3 H), 3.49 – 3.46 (m, 1 H), 3.43 (t, J = 6.6 Hz, 2 H), 2.59 – 2.54 (m, 1 H), 2.33 – 2.17 (m, 3 H), 2.09 (q, J = 7.3 Hz, 2 H), 2.04 – 1.98 (m, 4 H), 1.61 – 1.53 (m, 4 H), 1.44 – 1.39 (m, 2 H), 0.95 (t, J = 7.6 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.55, 161.73, 159.26, 137.83, 135.92, 135.04, 132.74, 132.62, 130.82, 129.34, 128.21, 125.19, 113.89, 72.70, 70.03, 55.41, 43.52, 30.49, 29.54, 28.90, 28.79, 27.29, 26.89, 26.31, 20.70, 14.45 ppm; HR-MS (ESI-TOF): calcd for C₂₈H₃₈O₃Na [M+Na]⁺: 445.2725, found: 445.2728.

(5Z,12E,17Z)-11-Oxoprosta-5,9,12,17-tetraen-1-oic acid (15): To a stirred solution of dienone



71 (20 mg, 47 μ mol, 1.0 equiv) in MeCN:H₂O (9:1, 0.4 mL) at 25 °C was dropwise added 4-(acetylamino)-2,2,6,6-tetramethyl-1-oxo-piperidinium tetrafluoroborate **72** (85 mg, 280 μ mol, 6.0 equiv). After

stirring for 30 min, the reaction mixture was diluted with a solution of H₂O (2 mL) and extracted with EtOAc (3×10 mL). The combined organic extracts were washed with brine (5 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:9) gave pure title compound (**15**, 6.9 mg, 21 µmol, 45 % yield) as a colorless oil.

15: $R_f = 0.40$ (hexanes:EtOAc, 1:9); $[\alpha]_D^{25} = +171.5$ (c = 1.00 in C_6H_6); IR (film): $v_{max} = 3007$, 2961, 2932, 1704, 1652, 1579, 1479, 1237, 679 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.48 (dd, J = 6.0, 2.4 Hz, 1 H), 6.58 (t, J = 8.0 Hz, 1 H), 6.34 (dd, J = 6.0, 1.8 Hz, 1 H), 5.48 – 5.43 (m, 1 H), 5.42 – 5.34 (m, 1 H), 5.32 – 5.27 (m, 2 H), 3.51 – 3.48 (m, 1 H), 2.57 (dt, J = 14.6, 5.5 Hz, 1 H), 2.33 (t, J = 7.6 Hz, 2 H), 2.31 – 2.19 (m, 3 H), 2.10 – 1.99 (m, 6 H), 1.68 (quint, J = 7.6 Hz, 2 H), 1.56

(quint, J = 7.6 Hz, 2 H), 0.94 (t, J = 7.6 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.94, 179.19, 161.68, 137.69, 136.20, 135.10, 132.74, 131.36, 128.17, 126.19, 43.37, 33.40, 30.38, 28.89, 28.74, 26.84, 26.68, 24.50, 20.68, 14.42 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₈O₃Na [M+Na]⁺: 339.1931, found: 339.1937.

Methyl (5Z,12E,17Z)-11-oxoprosta-5,9,12,17-tetraen-1-oate (16): To a stirred solution of A^{12} -PGJ₃ (15) (3.3 mg, 10 µmol, 1.0 equiv) in C₆H₆:MeOH (3:2, 0.5 mL) at 25 °C was dropwise added a solution of trimethylsilyl diazomethane (2.0 M in Et₂O, 10 µL, 20 µmol, 2.0 equiv) (yellow color persists). After stirring for 30 min, the reaction mixture was concentrated under reduced

pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, $6:1\rightarrow 3:2$) gave pure title compound (**16**, 3.0 mg, 9.0 µmol, 90 % yield) as a colorless oil.

16: $R_f = 0.53$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{25} = +162.5$ (c = 0.40 in C_6H_6); IR (film): $v_{max} = 3006$, 1932, 1737, 1702, 1654, 1581, 1436, 1365, 1215, 1173, 517 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.46 (dd, J = 6.0, 2.4 Hz, 1 H), 6.56 (t, J = 8.0 Hz, 1 H), 6.31 (dd, J = 6.0, 1.8 Hz, 1 H), 5.46 – 5.42 (m, 1 H), 5.41 – 5.27 (m, 3 H), 3.64 (s, 3 H), 3.50 – 3.47 (m, 1 H), 2.56 (dt, J = 15.1, 5.8 Hz, 1 H), 2.31 – 2.18 (m, 5 H), 2.08 (q, J = 7.4 Hz, 2 H), 2.04 – 1.98 (m, 4 H), 1.68 (quint, J = 7.6 Hz, 2 H), 1.57 (quint, J = 7.6 Hz, 2 H), 0.93 (t, J = 7.6 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.73, 173.94, 161.51, 137.69, 135.93, 135.09, 132.70, 131.48, 128.16, 126.02, 51.59, 43.36, 34.46, 30.37, 28.85, 28.74, 26.83, 26.76, 24.75, 20.66, 14.40 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₃₀O₃Na [M+Na]⁺: 353.2087, found: 353.2094.

Synthesis of Δ^{12} -PGJ₃ Propane Analogs **17** and **18**:

$(4S,5E) - 4 - \{(2Z) - 7 - [(4-Methoxybenzyl) oxy] hept - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl\} - 5 - propylidenecyclopent - 2 - en - 1 - yl] - 5 - propylidenecyclopent - 2 - en -$

one (75): To a stirred solution of diisopropylamine (60 µL, 0.42 mmol, 2.2 equiv) in THF (2 mL)

OPMB Me 75

at 0 °C was dropwise added *n*-butyl lithium (2.5 M in hexanes, 150 μ L, 0.38 mmol, 2.0 equiv). After stirring for 20 min at this temperature, the clear solution was cooled to -78 °C and a solution

of enone **57** (60 mg, 0.19 mmol, 1.0 equiv) in THF (1 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 15 min at this temperature, a solution of propionaldehyde **73** (21 μ L, 0.28 mmol, 1.5 equiv) in THF (1 mL) was added dropwise and stirring

at this temperature was continued for an additional 30 min. The reaction mixture was then quenched by addition of saturated aqueous NH₄Cl-solution (5 mL), diluted with EtOAc (25 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with EtOAc (2×15 mL), and the combined organic extracts were washed with brine (5 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereoisomers (55 mg, 0.15 mmol, 79 % yield) as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of the aldol product (55 mg, 0.15 mmol, 1.0 equiv) in CH₂Cl₂ (2 mL) at 25 °C was added DMAP (180 mg, 1.5 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (73 μ L, 3.0 mmol, 2.0 equiv). After stirring for 6 h at this temperature, the reaction mixture was quenched by addition of saturated aqueous NaHCO₃-solution (5 mL) and diluted with CH₂Cl₂ (25 mL). The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 10 mL), and the combined organic extracts were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 7:1) gave pure title compound (**75**, 42 mg, 0.12 mmol, 63 % yield for the two steps) as a colorless oil.

75: $R_f = 0.68$ (hexanes: EtOAc, 3:1); $[\alpha]_D^{25} = +141.2$ (c = 1.00 in C_6H_6); IR (film): $v_{max} = 2934$, 2857, 1702, 1655, 1613, 1513, 1460, 1301, 1247, 1099, 1034, 811 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.47 (dd, J = 6.2, 2.7 Hz, 1 H), 7.25 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.54 (t, J = 7.9 Hz, 1 H), 6.32 (dd, J = 6.0, 1.6 Hz, 1 H), 5.50 – 5.45 (m, 1 H), 5.34 – 5.30 (m, 1 H), 4.42 (s, 2 H), 3.80 (s, 3 H), 3.50 – 3.47 (m, 1 H), 3.43 (t, J = 6.5 Hz, 2 H), 2.56 (dt, J = 14.2, 5.0 Hz, 1 H), 2.33 – 2.25 (m, 2 H), 2.21 (dt, J = 14.8, 8.3 Hz, 1 H), 2.00 (q, J = 7.0 Hz, 2 H), 1.59 (quint, J = 7.6 Hz, 2 H), 1.41 (quint, J = 7.6 Hz, 2 H), 1.11 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 197.00, 161.70, 159.25, 137.47, 137.09, 135.03, 132.59, 130.81, 129.33, 125.20, 113.88, 72.69, 70.01, 55.40, 43.45, 30.50, 29.52, 27.27, 26.29, 22.75, 13.27 ppm; HR-MS (ESI-TOF): calcd for C₂₃H₃₀O₃Na [M+Na]⁺: 377.2087, found: 377.2098.

(5Z)-7-[(1S,5E)-4-Oxo-5-propylidenecyclopent-2-en-1-yl]hept-5-enoic acid (17): To a stirred solution of dienone 75 (10 mg, 30 μ mol, 1.0 equiv) in MeCN:H₂O (9:1, 0.4 mL) at 25 °C was dropwise added 4-(acetylamino)-2,2,6,6tetramethyl-1-oxo-piperidinium tetrafluoroborate **72** (54 mg, 15 μ mol, 6.0 equiv). After stirring for 30 min, the reaction mixture was diluted with H₂O (2 mL) and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (5 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:9) gave pure title compound (**17**, 4.2 mg, 17 μ mol, 57 % yield) as a colorless oil.

17: $R_f = 0.40$ (hexanes:EtOAc, 1:10); $[\alpha]_D^{25} = +142.5$ (c = 1.00 in C_6H_6); IR (film): $v_{max} = 3010$, 2966, 2934, 2874, 1728, 1700, 1641, 1578, 1215, 1150, 810 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.47 (dd, J = 6.2, 2.7 Hz, 1 H), 6.55 (t, J = 7.9 Hz, 1 H), 6.33 (dd, J = 6.0, 1.6 Hz, 1 H), 5.47 – 5.43 (m, 1 H), 5.38 – 5.34 (m, 1 H), 3.52 – 3.49 (m, 1 H), 2.57 (dt, J = 14.2, 5.3 Hz, 1 H), 2.33 (t, J = 7.6 Hz, 2 H), 2.32 – 2.26 (m, 2 H), 2.22 (dt, J = 15.2, 8.3 Hz, 1 H), 2.05 (q, J = 7.0 Hz, 2 H), 1.68 (quint, J = 7.6 Hz, 2 H), 1.10 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.94, 174.00, 161.54, 137.56, 136.99, 135.14, 131.50, 126.08, 43.34, 33.50, 30.42, 26.78, 24.78, 22.76, 13.27 ppm; HR-MS (ESI-TOF): calcd for C₁₅H₂₀O₃Na [M+Na]⁺: 271.1305, found: 271.1304.

Methyl (5Z)-7-[(1S,5E)-4-oxo-5-propylidenecyclopent-2-en-1-yl]hept-5-enoate (18): To a

stirred solution of compound **17** (10 mg, 40 μ mol, 1.0 equiv) in C₆H₆:MeOH (3:2, 0.5 mL) at 25 °C was dropwise added a solution of trimethylsilyl diazomethane (2.0 M in Et₂O, 30 μ L, 60 μ mol, 1.5 equiv)

(yellow color persists). After stirring for 30 min, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 2:1 \rightarrow 3:2) gave pure title compound (**18**, 9.0 mg, 36 µmol, 90 % yield) as a colorless oil. **18**: R_f=0.53 (hexanes:EtOAc, 1:1); $[\alpha]_D^{25}$ =+168.3 (*c*=0.30 in C₆H₆); IR (film): v_{max}=3009, 2950, 2874, 1736, 1702, 1654, 1580, 1436, 1212, 1151, 809 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.48 (dd, *J*=6.2, 2.7 Hz, 1 H), 6.55 (t, *J*=7.9 Hz, 1 H), 6.33 (dd, *J*=6.0, 1.6 Hz, 1 H), 5.47 – 5.43 (m, 1 H), 5.38 – 5.34 (m, 1 H), 3.66 (s, 3 H), 3.52 – 3.49 (m, 1 H), 2.57 (dt, *J*=14.2, 5.3 Hz, 1 H), 2.33 – 2.26 (m, 4 H), 2.22 (dt, *J*=15.2, 8.3 Hz, 1 H), 2.03 (q, *J*=7.5 Hz, 2 H), 1.67 (quint, *J*=7.6 Hz, 2 H), 1.11 (t, *J*=7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.93, 173.99, 161.53, 137.55, 136.98, 135.13, 131.50, 126.07, 51.64, 43.35, 33.50, 30.43, 26.79, 24.78, 22.77, 13.27 ppm; HR-MS (ESI-TOF): calcd for C₁₆H₂₂O₃Na [M+Na]⁺: 285.1461, found: 285.1472.

Synthesis of Trifluoromethyl- Δ^{12} -PGJ₃ Analog **19**, its Methyl Ester **20** and Lactone **21**:

tert-Butyl(dimethyl)({(3S,5Z)-8,8,8-trifluoro-1-[(4-methoxybenzyl)oxy]oct-5-en-3-yl}oxy)-

silane (78): To a stirred solution of IPPh₃(CH₂)₂CF₃ (77, 3.58 g, 7.38 mmol, 2.0 equiv) in THF PMBO, (26 mL) at 0 °C was added NaHMDS (1.0 M in THF, 6.97 mL,

 $_{\rm OTBS}$ 78 6.97 mmol, 1.9 equiv) and the resulting light orange solution was allowed to warm to 25 °C. After stirring for 1 h at this temperature, the orange solution was cooled to -78 °C and a solution of aldehyde³ 76 (1.30 g, 3.67 mmol, 1.0 equiv) in THF (2 × 5 mL) was added. After stirring for 5 h at this temperature, the reaction mixture was quenched by addition of saturated aqueous NH₄Cl-solution (25 mL). The phases were separated and the aqueous layer was extracted with Et₂O (3 × 50 mL), and the combined organic extracts were dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 8:2) gave pure title compound (**78**, 1.39 g, 3.21 mmol, 88 % yield).

78: $R_f = 0.60$ (hexanes:EtOAc, 10:1); $[\alpha]_D^{25} = +13.5$ (c = 1.00, C_6H_6); IR (film): $v_{max} = 3092$, 2953, 2935, 2858, 1613, 1514, 1251, 1033, 836, 677 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.25 (d, J = 8.5 Hz, 2 H), 6.88 (d, J = 8.5 Hz, 2 H), 5.79 – 5.75 (m, 1 H), 5.49 – 5.44 (m, 1 H), 4.44 (d, J = 11.4 Hz, 1 H), 4.38 (d, J = 11.4 Hz, 1 H), 3.91 (dt, J = 7.1, 5.4 Hz, 1 H), 3.80 (s, 3 H), 3.49 (t, J = 6.9 Hz, 2 H), 2.83 – 2.77 (m, 2 H), 2.22 (t, J = 6.9 Hz, 2 H), 1.77 – 1.65 (m, 2 H), 0.88 (s, 9 H) 0.04 (s, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 159.26, 132.61, 130.64, 129.40, 126.25 (q, J = 276.4 Hz), 118.65 (q, J = 3.5 Hz), 113.86, 72.77, 68.86, 66.64, 55.36, 36.95, 35.62, 32.52 (q, J = 32.5 Hz), 25.92, 18.12, -4.34, -4.66 ppm; HR-MS (ESI-TOF): calcd for C₂₂H₃₅F₃O₃Si [M+Na]⁺: 455.2200, found: 455.2198.

(3S,5Z)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-8,8,8-trifluorooct-5-en-1-ol (79): To a vigorously HO_{CF_3} stirred solution of PMB ether 78 (700 mg, 1.62 mmol, 1.0 equiv) in a mixture of CH₂Cl₂:H₂O (20:1, 6.0 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (551 mg, 2.43 mmol, 1.5 equiv). After stirring at this temperature for 5 h, the reaction mixture was diluted with Et₂O (10 mL), filtered through Celite, washed with Et₂O, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 3:1→2:1) yielded pure title compound (79, 460 mg, 1.47 mmol, 91 % yield) as a colorless oil. **79:** $R_f = 0.47$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +17.9$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 2952$, 2935, 2860, 1473, 1347, 1253, 1138, 1070, 836, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 5.78 – 5.68 (m, 1 H), 5.53 – 5.46 (m, 1 H), 4.03 – 3.94 (m, 1 H), 3.84 – 3.77 (m, 1 H), 3.75 – 3.69 (m, 1 H), 2.92 – 2.77 (m, 2 H), 2.30 (t, J = 7.0 Hz, 2 H), 2.11 (br s, 1 H), 1.82 – 1.73 (m, 1 H), 1.69 – 1.61 (m, 1 H), 0.89 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 132.22, 126.20 (q, J = 276.6 Hz), 119.09 (q, J = 3.5 Hz), 70.81, 60.17, 38.10, 35.23, 32.60 (q, J = 32.5 Hz), 25.92, 18.09, -4.31, -4.68 ppm; HR-MS (ESI) calcd for C₁₄H₂₈O₂F₃Si [M+H]⁺: 313.1805, found: 313.1793.

(3*S*,5*Z*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-8,8,8-trifluorooct-5-enal (80): To a stirred solution $H \xrightarrow[]{0} 0$ $\overline{O}TBS$ 80 of primary alcohol 79 (400 mg, 1.28 mmol, 1.0 equiv) in CH₂Cl₂ (6 mL) was added Dess–Martin periodinane (1.08 g, 2.56 mmol, 2.0 equiv) at 0 °C. The resulting mixture was stirred for 30 min at 0 °C and then allowed to warm to 25 °C. After stirring for 90 min, the reaction was quenched by addition of sat. aq. NaHCO₃ solution (3 mL) followed by sat. aq. Na₂S₂O₃ solution (3 mL). After stirring for 20 min, the phases were separated and the aq. layer was extracted with CH₂Cl₂ (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 20:1) yielded pure title compound (80, 300 mg, 0.973 mmol, 76% yield) as a colorless oil.

80: $R_f = 0.66$ (hexanes:EtOAc, 8:2); $[\alpha]_D^{25} = +13.7$ (c = 1.6, CHCl₃); FT-IR (neat): $v_{max} = 2956$, 2931, 2859, 1726, 1473, 1348, 1252, 1135, 1102, 1085, 835, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 9.78 (t, J = 2.1 Hz, 1 H), 5.78 – 5.70 (m, 1 H), 5.56 – 5.51 (m, 1 H), 4.27 (quint, J = 6.1 Hz, 1 H), 2.88 – 2.79 (m, 2 H), 2.55 – 2.50 (m, 2 H), 2.36 – 2.27 (m, 2 H), 0.86 (s, 9 H), 0.07 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 201.62, 131.54, 126.14 (q, J = 276.5 Hz), 119.86 (q, J = 3.5 Hz), 67.47, 50.63, 35.69, 32.55 (q, J = 32.5 Hz), 25.81, 18.06, -4.40, -4.74 ppm; HR-MS (ESI) calcd for C₁₄H₂₅F₃O₂SiNa [M+Na]⁺: 333.1468, found: 333.1463.

(5Z,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-20,20,20-trifluoro-1-[(4-methoxy-

benzyl)oxy]prosta-5,9,12,17-tetraen-11-one (82): To a stirred solution of diisopropylamine (240 μ L, 1.7 mmol, 2.1 equiv) in THF (8.0 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M



in hexanes, 650 μ L, 1.6 mmol, 2.0 equiv). After stirring for 20 min at this temperature, the clear solution was cooled to -78 °C and a solution of enone **57** (250 mg, 0.81 mmol, 1.0 equiv) in THF

(2.0 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 20 min at this temperature, a solution of aldehyde **80** (300 mg, 0.97 mmol, 1.2 equiv) in THF (2.0 mL) was added dropwise and stirring at this temperature was continued for an additional 15 min. The reaction was then quenched with sat. aq. NH₄Cl solution (5 mL), diluted with EtOAc (5 mL), and the mixture was allowed to warm to 25 °C. The phases were separated, the aq. layer was extracted with EtOAc (2 × 10 mL), and the combined organic extracts were washed with brine (10 mL), dried (Na₂SO₄), filtered, and concentrated. The crude mixture was filtered through a short column (SiO₂, hexanes:EtOAc, 17:3) to obtain a mixture of diastereomeric alcohols (**81**, 360 mg, 0.57 mmol) as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of the so obtained aldol product (360 mg, 0.57 mmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at 0 °C was added DMAP (700 mg, 5.7 mmol, 10 equiv), and then, methanesulfonyl chloride (88 μ L, 1.1 mmol, 2.0 equiv) dropwise. After stirring for 6 h at room temperature, the reaction was quenched by addition of sat. aq. NH₄Cl solution (10 mL) and diluted with CH₂Cl₂ (30 mL). The phases were separated, the aq. layer was extracted with CH₂Cl₂ (2 × 5 mL), and the combined organic layers were washed with H₂O (10 mL), dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 9:1) yielded pure title compound (**82**, 210 mg, 0.35 mmol, 43 % for the two steps) as a colorless oil.

82: $R_f = 0.50$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = +103.4$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 2930$, 2856, 1704, 1656, 1613, 1584, 1513, 1463, 1249, 1132, 1095, 836, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.49 (ddd, J = 6.0, 2.7, 1.0 Hz, 1 H), 7.25 (d, J = 9.0 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.56 (t, J = 7.8 Hz, 1 H), 6.33 – 6.31 (m, 1 H), 5.80 – 5.76 (m, 1 H), 5.53 – 5.46 (m, 2 H), 5.34 – 5.30 (m, 1 H), 4.42 (s, 2 H), 3.93 (quint, J = 5.9 Hz, 1 H), 3.80 (s, 3 H), 3.42 (t, J = 6.5 Hz, 3 H), 2.88 – 2.74 (m, 2 H), 2.60 – 2.56 (m, 1 H), 2.47 – 2.38 (m, 2 H), 2.30 – 2.22 (m, 2 H), 2.21 – 2.12 (m, 1 H), 2.03 – 1.95 (m, 2 H), 1.62 – 1.54 (m, 2 H), 1.41 (quint, J = 7.6 Hz, 2 H), 0.87 (s, 9 H), 0.05 (s, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.35, 161.87, 159.22, 139.20, 134.93, 134.07, 132.70, 132.09, 131.68, 129.34, 126.21 (q, J = 276.8 Hz), 125.13, 119.33 (q, J = 3.5 Hz), 113.86, 72.68, 70.97, 70.01, 55.39, 43.48, 37.03, 35.38, 32.60 (q, J = 32.6 Hz), 30.66, 29.54, 27.30, 26.31,

25.91, 18.14, -4.42, -4.51 ppm; HR-MS (ESI) calcd for C₃₄H₄₉O₄F₃SiNa [M+Na]⁺: 629.3244, found: 629.3240.

(5Z,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-20,20,20-trifluoro-1-hydroxyprosta-

5,9,12,17-tetraen-11-one (83): To a vigorously stirred solution of dienone 82 (100 mg,

OH OTBS 83 0.16 mmol, 1.0 equiv) in a mixture of $CH_2Cl_2:H_2O$ (20:1, 3.4 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4benzoquinone (56 mg, 0.24 mmol, 1.5 equiv). After stirring at this

temperature for 2 h, the reaction mixture was diluted with Et₂O (10 mL), filtered through Celite, washed with Et₂O, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, $3:1\rightarrow2:1$) yielded pure title compound (**83**, 74 mg, 0.15 mmol, 92 % yield) as a colorless oil.

83: $R_f = 0.13$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = +111.4$ (c = 1.02, CHCl₃); FT-IR (neat): $v_{max} = 3444$, 2930, 2858, 1702, 1654, 1580, 1463, 1347, 1253, 1200, 1135, 1083, 837, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.50 (dd, J = 5.5, 2.7 Hz, 1 H), 6.56 (t, J = 7.8 Hz, 1 H), 6.33 (dd, J = 6.0, 1.8 Hz, 1 H), 5.80 – 5.76 (m, 1 H), 5.53 – 5.48 (m, 2 H), 5.37 – 5.32 (m, 1 H), 3.96 – 3.92 (m, 1 H), 3.64 (t, J = 6.5 Hz, 2 H), 3.45 – 3.43 (m, 1 H), 2.89 – 2.74 (m, 2 H), 2.63 – 2.58 (m, 1 H), 2.48 – 2.39 (m, 2 H), 2.29 – 2.14 (m, 3 H), 2.04 – 2.00 (m, 2 H), 1.59 – 1.54 (m, 2 H), 1.45 – 1.39 (m, 2 H), 0.88 (s, 9 H), 0.06 (s, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.30, 161.72, 139.20, 134.93, 132.55, 132.03, 131.65, 126.29 (q, J = 276.3 Hz), 125.25, 119.35 (q, J = 3.4 Hz), 70.99, 62.82, 43.47, 37.03, 35.36, 32.56 (q, J = 32.6 Hz), 32.40, 30.67, 27.18, 25.90, 25.79, 18.11, -4.43, -4.53 ppm; HR-MS (ESI) calcd for C₂₆H₄₁O₃F₃SiNa [M+Na]⁺: 509.2669, found: 509.2661.

5,9,12,17-tetraen-1-oic acid (85): To a vigorously stirred solution of hydroxy dienone 83 (74 mg,



0.15 mmol, 1.0 equiv) in CH₂Cl₂ (2 mL) at 25 °C was added in one portion pyridinium chlorochromate (65 mg, 0.30 mmol, 2.0 equiv). After stirring for 2 h, the reaction mixture was diluted with Et₂O (5 mL),

filtered through Celite, washed with Et_2O , and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 4:1) gave the intermediate aldehyde **84**, which was immediately used in the next reaction.

To a vigorously stirred solution of aldehyde dienone 84 (66 mg, 0.140 mmol, 1.0 equiv) in t-BuOH (2 mL) at 25 °C were dropwise added sequentially 2-methyl-2-butene (0.46 mL, 4.1 mmol, 30 equiv), a solution of NaH₂PO₄ (0.3 M in H₂O, 1.36 mL, 0.41 mmol, 3.0 equiv) and a solution of NaClO₂ (80%, 46 mg, 0.41 mmol, 3.0 equiv) in H₂O (0.55 mL). After stirring for 30 min, the reaction mixture was diluted with a solution of NaH₂PO₄ (1.0 g) in H₂O (20 mL) and extracted with EtOAc (5×20 mL). The combined organic extracts were washed with brine (5 mL), dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, CH₂Cl₂:EtOH, $25:1 \rightarrow 20:1$) yielded pure title compound (85, 64 mg, 0.13 mmol, 84 % yield) as a colorless oil. **85:** $R_f = 0.40$ (CH₂Cl₂:EtOH, 19:1); $[\alpha]_D^{25} = +110.0$ (c = 1.07, CHCl₃); FT-IR (neat): $v_{max} = 3013$, 2954, 2929, 2857, 1705, 1654, 1462, 1360, 1251, 1134, 1082, 836, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.50 (dd, J = 6.5, 2.7 Hz, 1 H), 6.57 (t, J = 7.8 Hz, 1 H), 6.34 (dd, J = 6.0, 1.9 Hz, 1 H), 5.79 - 5.75 (m, 1 H), 5.53 - 5.45 (m, 2 H), 5.40 - 5.36 (m, 1 H), 3.97 - 3.93 (m, 1 H), 3.45 - 3.43 (m, 1 H), 2.89 - 2.74 (m, 2 H), 2.63 - 2.59 (m, 1 H), 2.48 - 2.39 (m, 2 H), 2.34 (t, J = 7.3 Hz, 2 H),2.30 - 2.21 (m, 2 H), 2.19 - 2.14 (m, 1 H), 2.08 - 2.04 (m, 2 H), 1.68 (quint, J = 7.0 Hz, 2 H), 0.88(s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.31, 178.61, 161.68, 139.10, 135.00, 132.00, 131.81, 131.43, 126.17, 126.11 (q, *J* = 279.1 Hz), 119.38 (q, *J* = 3.5 Hz), 71.04, 43.42, 37.04, 35.37, 33.30, 32.58 (q, J=32.6 Hz), 30.60, 26.69, 25.90, 24.53, 18.15, -4.44, -4.52 ppm; HR-MS (ESI) calcd for C₂₆H₃₉O₄F₃SiNa [M+Na]⁺: 523.2462, found: 523.2444.

(5Z,12E,15S,17Z)-20,20,20-Trifluoro-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oic acid (19):



To a stirred solution of Δ^{12} -PGJ₃-15-*t*-butyldimethylsilyl-ether CF₃ analog (**85**) (60 mg, 120 µmol, 1.0 equiv) in MeCN (0.8 mL) at 0 °C was dropwise added a solution of HF (50% aq., 440 µL, ca. 12.0 mmol,

ca. 100 equiv) in MeCN (0.8 mL). After stirring at this temperature for 45 min, the reaction was quenched by the addition of sat. brine (5 mL) and extracted with EtOAc (5×5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, CH₂Cl₂:EtOH, 20:1 \rightarrow 15:1) yielded pure title compound (**19**, 39 mg, 110 µmol, 90 % yield) as a colorless oil.

19: $R_f = 0.24$ (CH₂Cl₂:MeOH, 19:1); $[\alpha]_D^{25} = +89.8$ (c = 1.05, CHCl₃); FT-IR (neat): $v_{max} = 3423$, 2942, 1701, 1646, 1581, 1429, 1344, 1251, 1136, 1059, 916, 834 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ 7.57 (ddd, J = 6.0, 2.6, 1.1 Hz, 1 H), 6.57 (t, J = 7.8, 1 H), 6.34 (dd, J = 6.0, 1.9 Hz, 1 H),
6.07 (t, J = 11.4 Hz, 1 H), 5.82 – 5.78 (m, 1 H), 5.62 – 5.58 (m, 1 H), 5.52 – 5.47 (m, 1 H), 5.45 – 5.40 (m, 1 H), 3.96 – 3.92 (m, 1 H), 3.48 – 3.45 (m, 1 H), 2.91 – 2.85 (m, 2 H), 2.73 – 2.64 (m, 1 H), 2.62 – 2.58 (m, 1 H), 2.52 – 2.46 (m, 1 H), 2.37 – 2.32 (m, 4 H), 2.15 – 2.08 (m, 3 H), 1.70 (quint, J = 7.2 Hz, 2 H) ppm; ¹³C-NMR (125 MHz, CDCl₃) δ 196.40, 177.00, 161.91, 139.99, 134.97, 131.68, 131.52, 130.92, 126.08 (q, J = 275.7 Hz), 126.07, 120.71 (q, J = 3.5 Hz), 70.57, 43.73, 36.61, 34.82, 32.91, 32.43 (q, J = 32.6 Hz), 30.53, 26.54, 24.51 ppm; HR-MS (ESI) calcd for C₂₀H₂₅O₄F₃Na [M+Na]⁺: 409.1597, found: 409.1579.

Methyl (5*Z*,12*E*,15*S*,17*Z*)-20,20,20-trifluoro-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1oate (20): To a stirred solution of trifluoromethyl- Δ^{12} -PGJ₃ analog (19) (10 mg, 26 µmol,



e 1.0 equiv) in C₆H₆:MeOH (3:2, 1.0 mL) at 25 °C was added dropwise
 a solution of trimethylsilyl diazomethane (2 M in Et₂O, 20 μL, 40 pmol, 1.5 equiv) (yellow color persists). After stirring for 15 min,

the reaction mixture was concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, $3:1\rightarrow3:2$) yielded pure title compound (**20**, 6.1 mg, 15 µmol, 60 % yield) as a colorless oil.

20: $R_f = 0.32$ (hexanes:EtOAc, 2:1), $[\alpha]_D^{25} = +143.7$ (c = 0.80, C_6H_6), FT-IR (neat): $v_{max} = 3445$, 3011, 2930, 1735, 1720, 1700, 1651, 1580, 1437, 1349, 1252, 1135, 1065 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ 7.52 (ddd, J = 5.0, 2.6, 1.3 Hz, 1 H), 6.60 (t, J = 7.8 Hz, 1 H), 6.35 (dd, J = 6.1, 1.4 Hz, 1 H), 5.84 – 5.79 (m, 1 H), 5.62 – 5.57 (m, 1 H), 5.50 – 5.45 (m, 1 H), 5.38 – 5.33 (m, 1 H), 3.93 – 3.87 (m, 1 H), 3.66 (s, 3 H), 3.51 – 3.48 (m, 1 H), 2.93 – 2.83 (m, 1 H), 2.64 (dt, J = 15.1, 5.7 Hz, 1 H), 2.54 (dt, J = 14.4, 7.1 Hz, 1 H), 2.49 – 2.44 (m, 1 H), 2.33 – 2.17 (m, 5 H), 2.08 – 2.03 (m, 3 H), 1.70 – 1.65 (m, 2 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.39, 174.22, 161.85, 139.79, 135.07, 133.75, 131.77, 131.19, 126.17 (q, J = 276.3 Hz), 125.85, 120.48 (q, J = 3.5 Hz), 70.31, 51.72, 43.44, 36.87, 35.19, 33.46, 32.62 (q, J = 28.7 Hz), 30.40, 26.83, 24.76 ppm; HR-MS (ESI) calcd for C₂₁H₂₇F₃O₄Na [M+Na]⁺: 423.1754, found: 423.1738.

(5Z,12E,15S,17Z)-20,20,20-Trifluoro-1,15-epoxyprosta-5,9,12,17-tetraene-1,11-dione (21):



To a stirred solution of 2-methyl-6-nitrobenzoic anhydride (25.0 mg, 72.5 μ mol, 1.4 equiv) and 4-dimethylaminopyridine (37.9 mg, 311 μ mol, 6.0 equiv) in CH₂Cl₂ (20 mL) was added a solution of trifluoromethyl- Δ^{12} -PGJ₃ analog (**19**) (20.0 mg, 51.8 μ mol, 1.0 equiv) in CH₂Cl₂ (10 mL) at

25 °C dropwise via syringe pump over 15 h. After stirring for an additional 2 h, the reaction mixture was washed sequentially with sat. aq. NaHCO₃-solution (5 mL), aq. HCl (0.2 M, 10 mL), and sat. brine (10 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 3:1) yielded pure title compound (**21**, 11.6 mg, 31.6 µmol, 62 % yield) as a colorless oil.

21: $R_f = 0.35$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +57.4$ (c = 0.9 in C₆H₆); IR (film): $v_{max} = 3008$, 2921, 1729, 1704, 1657, 1581, 1536, 1456, 1349, 1238, 1151, 994 cm⁻¹; ¹H-NMR (600 MHz, C₆D₆) δ 6.74 (dd, J = 6.3, 2.6 Hz, 1 H), 6.56 – 6.51 (m, 1 H), 6.19 (dd, J = 6.0, 1.9 Hz, 1 H), 5.41 – 5.35 (m, 1 H), 5.32 – 5.26 (m, 1 H), 5.18 – 5.13 (m, 1 H), 5.08 – 5.02 (m, 1 H), 4.94 (dtd, J = 9.1, 6.3, 2.6 Hz, 1 H), 3.17 – 3.15 (m, 1 H), 2.52 – 2.41 (m, 3 H), 2.35 – 2.21 (m, 2 H), 2.08 – 2.02 (m, 3 H), 1.96 – 1.91 (m, 2 H), 1.89 – 1.85 (m, 1 H), 1.80 – 1.74 (m, 1 H), 1.33 – 1.22 (m, 2 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 194.69, 172.27, 159.69, 140.45, 135.61, 131.80, 130.91, 130.24, 126.60 (q, J = 276.3 Hz), 125.29, 120.19 (q, J = 3.5 Hz), 72.13, 43.13, 33.55, 32.67, 32.28 (q, J = 29.6 Hz), 32.13, 28.39, 26.00, 24.54 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₃O₃F₃Na [M+Na]⁺: 391.1491, found: 391.1492.

Synthesis of 17,18-Dihydro- Δ^{12} -PGJ₃ Analog (22), its Methyl Ester (23) and Lactone (24):

(3S)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}oct-5-yn-1-ol (87): To a vigorously stirred solution of ^{HO} ^E ^{BT} ^{BT} ^E ^{BT}

this temperature before being quenched by the addition of saturated aqueous NaHCO₃-solution (10 mL). The mixture was stirred vigorously for 30 min, the layers were separated, and the aqueous layer was extracted with Et₂O (3×100 mL). The combined organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 9:1) gave pure title compound (**87**, 458 mg, 1.75 mmol, 90 % yield) as a light yellow oil.

87: $R_f = 0.50$ (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = +26.7$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 3362$, 2949, 2929, 2857, 1472, 1462, 1254, 1095, 1063, 1021, 834, 775 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ 4.01 (dddd, J = 7.7, 6.6, 5.4, 3.9 Hz, 1 H), 3.83 (ddd, J = 10.8, 8.3, 4.3 Hz, 1 H), 3.73 (ddd, J = 10.8, 5.9, 4.9 Hz, 1 H), 2.41 – 2.30 (m, 3 H), 2.17 – 2.11 (m, 2 H), 1.95 (dddd, J = 14.2, 8.4, 4.9, 3.8 Hz,

1 H), 1.78 (dddd, *J*=14.2, 6.7, 5.8, 4.3 Hz, 1 H), 1.09 (t, *J*=7.6 Hz, 3 H), 0.88 (s, 9 H), 0.10 (s, 6 H) ppm; ¹³C-NMR (125 MHz, CDCl₃) δ83.96, 75.96, 71.03, 60.18, 37.80, 27.41, 25.89, 18.09, 14.28, 12.55, -4.42, -4.75 ppm; HR-MS (ESI) calcd for C₁₄H₂₉O₂Si [M+H]⁺: 257.1931, found: 257.1925.

(3S)-3-{[tert-Butyl(dimethyl)silyl]oxy}oct-5-ynal (88): To a solution of primary alcohol 87



(80 mg, 0.31 mmol) in CH₂Cl₂ (4 mL) at 0 °C was added Dess–Martin periodinane (200 mg, 0.47 mmol, 1.5 equiv). The reaction mixture was warmed to 25 °C and stirred for 2 h. The reaction was then quenched with

sat. aq. Na₂S₂O₃ (4 mL) and sat. aq. NaHCO₃ (4 mL) and stirred for 10 min. The layers were separated, and the aqueous phase was extracted with CH₂Cl₂ (10 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 19:1 \rightarrow 9:1) yielded the title aldehyde (**88**, 69 mg, 0.27 mmol, 88 % yield) as a colorless oil.

88: $R_f = 0.60$ (hexanes:EtOAc, 4:1), $[\alpha]_D^{25} = +22.7$ (c = 1.0, CHCl₃), FT-IR (neat): $v_{max} = 2955$, 2930, 2857, 1726, 1472, 1463, 1253, 1101, 1004, 835, 775 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ 9.81 (dd, J = 2.8, 1.9 Hz, 1 H), 4.29 (dddd, J = 8.0, 7.2, 5.0, 4.4 Hz, 1 H), 2.72 (ddd, J = 16.0, 4.4, 1.9 Hz, 1 H), 2.61 (ddd, J = 16.0, 7.2, 2.8 Hz, 1 H), 2.41 (ddt, J = 16.4, 4.9, 2.4 Hz, 1 H), 2.32 (ddt, J = 16.4, 8.0, 2.4 Hz, 1 H), 2.17 – 2.11 (m, 2 H), 1.10 (t, J = 7.5 Hz, 3 H), 0.85 (s, 9 H), 0.09 (s, 3 H), 0.06 (s, 3 H) ppm; ¹³C-NMR (125 MHz, CDCl₃) δ 201.88, 84.75, 75.32, 67.62, 50.57, 28.23, 25.82, 18.08, 14.19, 12.52, -4.37, -4.74 ppm; HR-MS (ESI) calcd for C₁₄H₂₇O₂Si [M+H]⁺: 255.1775, found: 255.1779.

(5Z,12E,15R)-15-{[tert-Butyl(dimethyl)silyl]oxy}-1-[(4-methoxybenzyl)oxy]prosta-5,9,12-

trien-17-yn-11-one (90): To a stirred solution of diisopropylamine (300 µL, 2.10 mmol, 2.1 equiv)



in THF (8 mL) at 0 °C was added dropwise *n*-butyl lithium (2.5 M in hexanes, 0.800 mL, 2.00 mmol, 2.0 equiv). After stirring for 20 min at this temperature, the clear solution was cooled to -78 °C, and a solution

of enone **57** (314 mg, 1.00 mmol, 1.0 equiv) in THF (2.0 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 20 min at this temperature, a solution of

aldehyde **88** (304 mg, 1.20 mmol, 1.2 equiv) in THF (2.0 mL) was added dropwise, and stirring at this temperature was continued for an additional 30 min. The reaction was then quenched by the addition of sat. aq. NH₄Cl solution (8 mL), diluted with EtOAc (8 mL), and allowed to warm to 25 °C. The phases were separated, the aq. layer was extracted with EtOAc (8 mL), and the combined organic extracts were washed with brine (8 mL), dried (Na₂SO₄), filtered, and concentrated. The crude aldol product was filtered through a short column (SiO₂, hexanes:EtOAc, 9:1 \rightarrow 3:1) to obtain a mixture of diastereomeric alcohols (**89**, 460 mg, 0.800 mmol) as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of the so-obtained aldol product **89** (460 mg, 0.80 mmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at 0 °C was added DMAP (0.977 g, 8.00 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (124 μ L, 1.61 mmol, 2.0 equiv). After stirring for 6 h at room temperature, the reaction was quenched by the addition of sat. aq. NH₄Cl solution (10 mL) and diluted with CH₂Cl₂ (30 mL). The phases were separated, and the organic layer was washed with H₂O (10 mL), dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 19:1 \rightarrow 9:1 \rightarrow 4:1) yielded pure title compound (**90**, 198 mg, 0.360 mmol, 36% for the two steps) as a colorless oil.

90: $R_f = 0.65$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +97.1$ (c = 0.86, CHCl₃), FT-IR (neat): $v_{max} = 2929$, 2855, 1704, 1656, 1613, 1512, 1246, 1095, 1036, 835, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.49 (ddd, J = 6.0, 2.6, 1.0 Hz, 1 H), 7.25 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.64 – 6.61 (m, 1 H), 6.31 (dd, J = 6.0, 1.8 Hz, 1 H), 5.51 – 5.45 (m, 1 H), 5.37 – 5.31 (m, 1 H), 4.42 (s, 2 H), 3.93 (tt, J = 6.6, 5.3 Hz, 1 H), 3.80 (s, 3 H), 3.50 – 3.47 (m, 1 H), 3.42 (t, J = 6.5 Hz, 2 H), 2.67 – 2.59 (m, 2 H), 2.50 (dt, J = 14.6, 6.8 Hz, 1 H), 2.33 – 2.29 (m, 2 H), 2.21 – 2.11 (m, 3 H), 1.99 (q, J = 7.6 Hz, 2 H), 1.61 – 1.56 (m, 2 H), 1.43 – 1.37 (m, 2 H), 1.09 (t, J = 7.6 Hz, 3 H), 0.87 (s, 9 H), 0.08 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.42, 161.86, 159.21, 139.20, 134.92, 132.55, 132.22, 130.78, 129.33, 125.38, 113.85, 84.15, 75.97, 72.68, 70.92, 70.02, 55.39, 43.49, 36.63, 30.73, 29.53, 27.96, 27.28, 26.32, 25.91, 18.18, 14.30, 12.56, -4.47, -4.56 ppm; HR-MS (ESI) calcd for C₃₄H₅₀O₄SiNa [M+Na]⁺: 573.3371, found: 573.3344.

(5Z,12E,15R)-15-{[tert-Butyl(dimethyl)silyl]oxy}-1-hydroxyprosta-5,9,12-trien-17-yn-11-

one (91): To a vigorously stirred solution of dienone 90 (25 mg, 0.045 mmol, 1.0 equiv) in a



mixture of $CH_2Cl_2:H_2O$ (10:1, 1.1 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (15 mg, 0.068 mmol, 1.5 equiv). After stirring at this temperature for 45 min, an additional

portion of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (5.0 mg, 0.023 mmol, 0.5 equiv) was added. After stirring for an additional 60 min, the reaction mixture was diluted with Et₂O (3 mL), filtered through Celite, washed with Et₂O, and concentrated to a volume of ca. 0.5 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 9:1 \rightarrow 3:1 \rightarrow 3:2) yielded pure title compound (**91**, 19 mg, 0.044 mmol, 98 % yield) as a colorless oil.

91: $R_f = 0.30$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +121.2$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 3434$, 2928, 2856, 1700, 1652, 1580, 1462, 1252, 1090, 967, 835, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.51 (ddd, J = 6.0, 2.6, 1.0 Hz, 1 H), 6.62 (ddt, J = 8.4, 7.1, 1.3 Hz, 1 H), 6.32 (dd, J = 6.0, 1.8 Hz, 1 H), 5.51 – 5.46 (m, 1 H), 5.38 – 5.33 (m, 1 H), 3.94 (tt, J = 6.7, 5.4 Hz, 1 H), 3.63 (t, J = 6.5 Hz, 2 H), 3.52 – 3.48 (m, 1 H), 2.69 – 2.60 (m, 2 H), 2.50 (dt, J = 14.6, 6.8 Hz, 1 H), 2.33 – 2.29 (m, 2 H), 2.22 – 2.11 (m, 3 H), 2.02 (t, J = 7.5 Hz, 2 H), 1.65 – 1.53 (m, 3 H), 1.44 – 1.38 (m, 2 H), 1.09 (t, J = 7.5 Hz, 3 H), 0.87 (s, 9 H), 0.08 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.49, 161.88, 139.21, 134.95, 132.45, 132.31, 125.51, 84.19, 75.96, 70.93, 62.86, 43.52, 36.68, 32.44, 30.75, 27.97, 27.21, 25.92, 25.84, 18.20, 14.30, 12.57, -4.51, -4.55 ppm; HR-MS (ESI) calcd for C₂₆H₄₂O₃SiNa [M+Na]⁺: 453.2795, found: 453.2788.

(5Z,12E,15R)-15-{[*tert*-Butyl(dimethyl)silyl]oxy}-11-oxoprosta-5,9,12-trien-17-yn-1-oic acid (93): To a vigorously stirred solution of alcohol 91 (19 mg, 0.044 mmol, 1.0 equiv) in CH₂Cl₂



(1 mL) at 25 °C was added in one portion pyridinium chlorochromate (19 mg, 0.088 mmol, 2.0 equiv). After stirring for 40 min, the reaction mixture was filtered through a short pad of SiO₂ (hexanes:EtOAc, 7:3)

and concentrated to give intermediate aldehyde **92** (18 mg, 0.042 mmol, 95 % yield), which was used directly in the next step.

To a vigorously stirred solution of aldehyde **92** (18 mg, 0.042 mmol, 1.0 equiv) in *t*-BuOH (0.8 mL) and H₂O (0.6 mL) at 25 °C were added sequentially 2-methyl-2-butene (47 μ L, 0.44 mmol, 10 equiv), NaH₂PO₄ (10 mg, 0.066 mmol, 1.5 equiv) and NaClO₂ (6.0 mg,

0.066 mmol, 1.5 equiv). After stirring for 20 min, the reaction mixture was diluted with a solution of NaH₂PO₄ (500 mg) in H₂O (10 mL) and extracted with EtOAc (2 × 10 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, CH₂Cl₂:EtOH, 49:1 \rightarrow 19:1) yielded pure title compound (**93**, 16 mg, 0.035 mmol, 80% for the two steps) as a colorless oil.

93: $R_f = 0.50$ (CH₂Cl₂:EtOH, 19:1); $[\alpha]_D^{25} = +122.8$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 2929$, 2856, 1705, 1654, 1462, 1433, 1361, 1251, 1091, 836, 808, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.50 (ddd, J = 6.0, 2.6, 1.0 Hz, 1 H), 6.63 (ddt, J = 8.3, 7.0, 1.2 Hz, 1 H), 6.34 (dd, J = 6.0, 1.8 Hz, 1 H), 5.49 – 5.37 (m, 2 H), 3.94 (quint, J = 6.0 Hz, 1 H), 3.52 – 3.48 (m, 1 H), 2.69 – 2.60 (m, 2 H), 2.51 (dt, J = 14.7, 6.7 Hz, 1 H), 2.36 – 2.29 (m, 4 H), 2.21 – 2.11 (m, 3 H), 2.06 (q, J = 7.5 Hz, 2 H), 1.71 – 1.65 (m, 2 H), 1.09 (t, J = 7.5 Hz, 3 H), 0.87 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.48, 178.71, 161.77, 139.12, 135.04, 132.41, 131.35, 126.42, 84.23, 75.94, 71.00, 43.46, 36.67, 33.38, 30.69, 27.93, 26.70, 25.92, 24.58, 18.22, 14.29, 12.57, -4.48, -4.54 ppm; HR-MS (ESI) calcd for C₂₆H₄₀O₄SiNa [M+Na]⁺: 467.2588, found: 467.2571.

(5Z,12E,15R)-15-Hydroxy-11-oxoprosta-5,9,12-trien-17-yn-1-oic acid (22): To a stirred



solution of TBS ether **93** (100 mg, 0.23 mmol, 1.0 equiv) in MeCN (2.0 mL) at 0 °C was added dropwise a solution of HF (50% aq., 570 μ L, ca. 23 mmol, ca. 100 equiv) in MeCN (0.2 mL). After stirring for 30 min, the reaction was

quenched by addition of sat. brine (3 mL) and extracted with EtOAc (5 mL). The organic extract was dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 0.5 mL (not to dryness!). Flash column chromatography (SiO₂, CH₂Cl₂:EtOH, 99:1 \rightarrow 97:3 \rightarrow 95:5 \rightarrow 93:7) yielded pure title compound (**22**, 56 mg, 0.17 mmol, 74 % yield) as a colorless oil.

22: $R_f = 0.40$ (CH₂Cl₂:EtOH, 19:1); $[\alpha]_D^{25} = +88.0$ (c = 0.62, CHCl₃); FT-IR (neat): $v_{max} = 3407$, 2974, 2935, 1698, 1646, 1433, 1406, 1237, 1182, 1061, 1047 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.55 (dd, J = 6.0, 2.5 Hz, 1 H), 6.57 (t, J = 7.7 Hz, 1 H), 6.35 (d, J = 6.0 Hz, 1 H), 5.51 – 5.47 (m, 1 H), 5.44 – 5.40 (m, 1 H), 3.95 (quint, J = 6.3 Hz, 1 H), 3.52 – 3.48 (m, 1 H), 2.70 (dt, J = 12.7, 5.9 Hz, 1 H), 2.65 – 2.54 (m, 2 H), 2.52 – 2.44 (m, 2 H), 2.40 – 2.33 (m, 3 H), 2.20 – 2.09 (m, 5 H), 1.72 – 1.67 (m, 2 H), 1.13 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.42, 177.01, 161.86, 139.93, 135.06, 131.67, 130.93, 126.18, 85.64, 74.58, 69.67, 43.72, 35.85, 33.05,

30.61, 27.22, 26.62, 24.62, 14.30, 12.57 ppm; HR-MS (ESI) calcd for C₂₀H₂₆O₄Na [M+Na]⁺: 353.1723, found: 353.1729.

Methyl (5Z,12E,15R)-15-hydroxy-11-oxoprosta-5,9,12-trien-17-yn-1-oate (23): To a stirred solution of 17,18-didehydro- Δ^{12} -PGJ₃ (22) (2.0 mg, 6.1 µmol, 1.0 equiv) in C₆H₆:MeOH (3:2, 0.25 mL) at 25 °C was added dropwise a solution of trimethylsilyl diazomethane (2 M in Et₂O, 6.0 µL, 12 µmol, 2.0 equiv)

(yellow color persists). After stirring for 15 min, the reaction mixture was concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, $3:1\rightarrow3:2$) yielded the pure title compound (**23**, 1.8 mg, 5.2 µmol, 90% yield) as a colorless oil.

23: $R_f = 0.26$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = +129.2$ (c = 0.18, C_6H_6); FT-IR (neat): $v_{max} = 3444$, 2922, 2852, 1735, 1699, 1651, 1580, 1436, 1367, 1209, 1176, 1068 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.51 (dd, J = 6.0, 2.6 Hz, 1 H), 6.61 (t, J = 7.8 Hz, 1 H), 6.35 (dd, J = 6.0, 1.8 Hz, 1 H), 5.51 – 5.44 (m, 1 H), 5.36 (dtt, J = 10.9, 8.2, 1.6 Hz, 1 H), 3.91 (dt, J = 6.5, 5.3 Hz, 1 H), 3.67 (s, 3 H), 3.58 – 3.52 (m, 1 H), 2.65 – 2.61 (m, 1 H), 2.57 (dd, J = 7.8, 6.4 Hz, 2 H), 2.47 (ddt, J = 16.5, 4.8, 2.4 Hz, 1 H), 2.35 (ddt, J = 16.5, 6.2, 2.4 Hz, 1 H), 2.31 (t, J = 7.3 Hz, 2 H), 2.28 – 2.21 (m, 2 H), 2.19 (qt, J = 7.5, 2.4 Hz, 2 H), 2.05 (q, J = 7.0 Hz, 1 H), 1.67 (quint, J = 7.4 Hz, 2 H), 1.13 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.39, 174.13, 161.78, 139.71, 135.09, 131.72, 131.16, 125.95, 85.50, 74.74, 69.44, 51.73, 43.41, 36.08, 33.50, 30.46, 27.51, 26.85, 24.81, 14.34, 12.58 ppm; HR-MS (ESI) calcd for C₂₁H₂₈O₄Na [M+Na]⁺: 367.1880, found: 367.1883.

(5Z,12E,15R)-1,15-Epoxyprosta-5,9,12-trien-17-yne-1,11-dione (24): To a stirred solution of



2-methyl-6-nitrobenzoic anhydride (23 mg, 63 μ mol, 1.4 equiv) and 4-dimethylaminopyridine (33 mg, 270 μ mol, 6.0 equiv) in CH₂Cl₂ (20 mL) was added a solution of 17,18-didehydro- Δ^{12} -PGJ₃ (**22**) (15 mg, 45 μ mol, 1.0 equiv)

in CH₂Cl₂ (10 mL) at 25 °C dropwise via syringe pump over 15 h. After stirring for an additional 2 h, the reaction mixture was washed sequentially with sat. aq. NaHCO₃-solution (10 mL), aq. HCl (0.2 M, 10 mL), and sat. brine (10 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 3:1) yielded pure title compound (**24**, 7.0 mg, 22 µmol, 50 % yield) as a colorless oil.

24: $R_f = 0.40$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +42.5$ (c = 0.7 in C_6H_6); IR (film): $v_{max} = 2924$, 2855, 1726, 1703, 1655, 1581, 1535, 1457, 1440, 1348, 1252, 1132, 1084, 1057, 1018, 920, 804 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 6.72 (ddd, J = 6.2, 2.6, 1.0 Hz, 1 H), 6.58 – 6.50 (m, 1 H), 6.19 (dd, J = 6.1, 1.9 Hz, 1 H), 5.14 (tdd, J = 10.9, 5.0, 1.6 Hz, 1 H), 5.05 (tdd, J = 10.7, 4.9, 1.8 Hz, 1 H), 4.99 (dddd, J = 9.4, 6.9, 4.3, 2.8 Hz, 1 H), 3.18 – 3.12 (m, 1 H), 2.75 (ddd, J = 14.7, 10.3, 4.6 Hz, 1 H), 2.62 (ddd, J = 14.8, 12.0, 10.6 Hz, 1 H), 2.57 – 2.47 (m, 2 H), 2.25 (ddt, J = 16.7, 4.6, 2.4 Hz, 1 H), 2.09 – 1.91 (m, 6 H), 1.77 – 1.67 (m, 1 H), 1.38 – 1.31 (m, 1 H), 1.25 – 1.18 (m, 1 H), 0.98 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 194.77, 172.12, 159.70, 140.34, 135.73, 131.96, 130.39, 125.13, 84.52, 74.93, 71.14, 42.92, 33.34, 32.67, 28.38, 25.94, 24.69, 24.52, 14.35, 12.74 ppm; HR-MS (ESI-TOF): calcd for $C_{20}H_{24}O_3Na$ [M+Na]⁺: 335.1618, found: 335.1615.

Synthesis of Δ^{12} -PGJ₃ Analog (12), its Methyl Ester (13) and Lactone (14):

(3R,4E)-3-{[tert-Butyl(dimethyl)silyl]oxy}-5-[3-(trifluoromethyl)phenyl]pent-4-en-1-ol (96):



To a stirred solution of $\{3-(trifluoromethyl)benzyl\}$ triphenylphosphonium bromide **95** (3.75 g, 7.50 mmol, 1.5 equiv) in THF (30 mL) at 0 °C was added dropwise *n*-butyl lithium (1.6 M in hexanes, 4.69 mL, 7.50 mmol, 1.5 equiv). After stirring for 2 h at this temperature, the resulting bright orange solution

was cooled to -78 °C and a solution of lactol **94**⁴ (1.09 g, 5.00 mmol, 1.0 equiv) in THF (5 mL) was added dropwise. After stirring at this temperature for 30 min, the reaction mixture was warmed to 25 °C over the course of 2 h and stirred for an additional 24 h at 40 °C. The reaction mixture was then quenched with sat. aqueous NH₄Cl-solution (50 mL) and extracted with CH₂Cl₂ (3 × 30 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, pentane:Et₂O, 8:1) yielded pure title compound as a mixture of *cis* and *trans* isomers (**96**, ca. 1:2, 1.29 g, 3.60 mmol, 72 % yield) as a colorless oil.

96 (*cis*-isomer): $R_f = 0.46$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +13.5$ (c = 1.7 in C_6H_6); IR (film): $v_{max} = 3421$, 3011, 2954, 2931, 2887, 2859, 1472, 1329, 1255, 1165, 1128, 1073, 1033, 837, 777 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.53 (d, J = 7.8 Hz, 1 H), 7.48 – 7.45 (m, 2 H), 7.38 (d, J = 7.6 Hz, 1 H), 6.46 (d, J = 11.7 Hz, 1 H), 5.84 (dd, J = 11.9, 9.1 Hz, 1 H), 4.86 – 4.82 (m, 1 H), 3.90 – 3.86 (m, 1 H), 3.81 – 3.79 (m, 1 H), 2.31 (t, J = 5.0 Hz, 1 H), 1.95 – 1.86 (m, 2 H), 0.83 (s, 9 H), -0.07 (s, 3 H), -0.11 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 137.53, 137.23, 131.80, 130.85 (q, J = 32.3 Hz), 128.89, 127.19, 125.41 (q, J = 3.8 Hz), 124.11 (q, J = 276.3 Hz), 123.93

(q, *J*=3.5 Hz), 68.05, 60.30, 39.61, 25.80, 18.07, -4.28, -5.06 ppm; HR-MS (ESI-TOF): calcd for C₁₈H₂₇F₃O₂SiNa [M+Na]⁺: 383.1634, found: 383.1634.

96 (*trans*-isomer): $R_f = 0.36$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +31.0$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 3366$, 3006, 2954, 2932, 2887, 2859, 1472, 1361, 1331, 1126, 1075, 1055, 1033, 835, 777 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.59 (s, 1 H), 7.53 (d, J = 7.7 Hz, 1 H), 7.49 (d, J = 7.8 Hz, 1 H), 7.43 (t, J = 7.7 Hz, 1 H), 6.59 (d, J = 15.9 Hz, 1 H), 6.30 (dd, J = 15.9, 6.0 Hz, 1 H), 4.51 – 4.45 (m, 1 H), 3.88 – 3.84 (m, 1 H), 3.77 – 3.74 (m, 1 H), 2.34 (s, 1 H), 1.96 – 1.91 (m, 1 H), 1.86 – 1.80 (m, 1 H), 0.94 (s, 9 H), 0.13 (s, 3 H), 0.08 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 137.64, 134.31, 131.14 (q, J = 32.3 Hz), 129.60, 129.14, 128.28, 124.18 (q, J = 3.8 Hz), 124.18 (q, J = 276.3 Hz), 123.10 (q, J = 3.5 Hz), 72.53, 60.11, 39.65, 25.93, 18.24, –4.20, –4.86 ppm; HR-MS (ESI-TOF): calcd for C₁₈H₂₇F₃O₂SiNa [M+Na]⁺: 383.1634, found: 383.1634.





stirred suspension of Pd-C (10 % Pd on carbon, 130 mg, 10 wt%) in MeOH (10 mL) were sequentially added a solution of t-butyldimethylsilyl ether **96** (1.3 g, 3.6 mmol, 1.0 equiv) in MeOH

(10 mL) at 25 °C. The suspension was degassed and purged with Ar three times, then the atmosphere was changed to H₂ (balloon). After vigorous stirring for 3 h at the same temperature, the reaction mixture was filtered through Celite, washed with EtOAc, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 20:1) yielded pure title compound (**97**, 1.2 g, 3.3 mmol, 91 % yield) as a colorless oil.

97: $R_f = 0.36$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +1.8$ (c = 0.8 in C_6H_6); IR (film): $v_{max} = 3366$, 2953, 2931, 2859, 1463, 1361, 1256, 1163, 1073, 1033, 836, 775, 702 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.47 - 7.42 (m, 2 H), 7.40 (t, J = 7.6 Hz, 1 H), 7.36 (d, J = 7.7 Hz, 1 H), 4.00 - 3.97 (m, 1 H), 3.87 - 3.82 (m, 1 H), 3.77 - 3.73 (m, 1 H), 2.75 - 2.66 (m, 2 H), 2.17 (t, J = 5.1 Hz, 1 H), 1.89 - 1.84 (m, 3 H), 1.78 - 1.72 (m, 1 H), 0.92 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 143.16, 131.78, 130.83 (q, J = 32.3 Hz), 128.91, 125.05 (q, J = 3.8 Hz), 124.30 (q, J = 276.3 Hz), 122.85 (q, J = 3.5 Hz), 70.84, 60.12, 38.59, 38.14, 31.58, 25.92, 18.09, -4.36, -4.53 ppm; HR-MS (ESI-TOF): calcd for $C_{18}H_{30}F_3O_2Si$ [M+H]⁺: 363.1963, found: 363.1958.

(3S)-3-{[tert-Butyl(dimethyl)silyl]oxy}-5-[3-(trifluoromethyl)phenyl]pentanal (98): To a



stirred solution of primary alcohol **97** (500 mg, 1.38 mmol, 1.0 equiv) in CH₂Cl₂ (5 mL) was added Dess–Martin periodinane (1.15 mg, 2.76 mmol, 2.0 equiv) at 0 °C. The resulting mixture was stirred for 30 min at the same

temperature and then allowed to warm to 25 °C. After stirring for 30 min, the reaction was quenched by sequential addition of sat. aqueous NaHCO₃ solution (2.0 mL) and sat. aqueous Na₂S₂O₃ solution (2.0 mL). After stirring for 20 min, the phases were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 20:1) yielded pure title compound (**98**, 410 mg, 1.14 mmol, 83 % yield) as a colorless oil.

98: $R_f = 0.60$ (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = -2.2$ (c = 3.7 in C_6H_6); IR (neat): $v_{max} = 2954$, 2931, 2859, 1726, 1450, 1328, 1254, 1163, 1073, 1033, 1005, 835, 775, 702 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 9.46 (t, J = 2.0 Hz, 1 H), 7.38 (s, 1 H), 7.26 (d, J = 7.6 Hz, 1 H), 6.94 (dt, J = 15.2, 7.7 Hz, 2 H), 3.91 (quint, J = 5.7 Hz, 1 H), 2.42 – 2.30 (m, 2 H), 2.20 – 2.26 (m, 1 H), 2.02 – 1.98 (m, 1 H), 2.54 – 1.49 (m, 1 H), 1.02 – 0.99 (m, 1 H), 0.91 (m, 9 H), -0.02 (s, 6 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 199.70, 143.23, 131.92, 131.06 (q, J = 32.3 Hz), 129.20, 125.30 (q, J = 3.8 Hz), 125.09 (q, J = 276.3 Hz), 123.10 (q, J = 3.5 Hz), 67.48, 50.94, 39.32, 31.37, 25.97, 18.19, -4.47, -4.50 ppm; HR-MS (ESI-TOF): calcd for $C_{18}H_{28}F_3O_2Si$ [M+H]⁺: 361.1805, found: 361.1789.

(4*S*,5*E*)-5-{(3*S*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-5-[3-(trifluoromethyl)phenyl]pentylidene}-4-{(2*Z*)-7-[(4-methoxybenzyl)oxy]hept-2-en-1-yl}cyclopent-2-en-1-one (100): To a stirred



solution of diisopropylamine (200 μ L, 1.44 mmol, 2.1 equiv) in THF (5 mL) at 0 °C was dropwise added *n*-butyl lithium (1.6 M in hexanes, 875 μ L, 1.40 mmol, 2.0 equiv). After stirring for 20 min at this

temperature, the clear solution was cooled to -78 °C and a solution of enone **57** (220 mg, 0.700 mmol, 1.0 equiv) in THF (4 mL) was added dropwise. After stirring for an additional 20 min at this temperature, a solution of aldehyde **98** (327 mg, 0.910 mmol, 1.3 equiv) in THF (4 mL) was added dropwise and stirring at this temperature was continued for an additional 20 min. The reaction mixture was then quenched by the addition of saturated aqueous NH₄Cl-solution (75 mL), diluted with EtOAc (75 mL), and allowed to warm to 25 °C. The phases were separated, the

aqueous layer was extracted with EtOAc (2×75 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereoisomers (**99**, 350 mg, 0.518 mmol, 74 % yield) as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of the aldol product (350 mg, 0.518 mmol, 1.0 equiv) in CH₂Cl₂ (6 mL) at -10 °C was added DMAP (634 mg, 5.18 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (120 µL, 1.56 mmol, 2.0 equiv). After stirring for 30 min at this temperature, the reaction mixture was allowed to warm to 25 °C and stirred for 6 h. The reaction mixture was quenched by addition of saturated aqueous NaHCO₃-solution (10 mL), diluted with CH₂Cl₂ (50 mL), the phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 50 mL), and the combined organic layers were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 7:1) gave pure title compound (**100**, 210 mg, 0.320 mmol, 45 % yield for the two steps) as a colorless oil.

100: $R_f = 0.53$ (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = +34.2$ (c = 0.4 in C_6H_6); IR (film): $v_{max} = 3006$, 2951, 2935, 2858, 1704, 1657, 1513, 1328, 1249, 1125, 1033, 836, 776 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 7.42 (s, 1 H), 7.26 – 7.24 (m, 3 H), 6.99 (d, J = 7.7 Hz, 1 H), 6.94 – 6.91 (m, 2 H), 6.84 – 6.78 (m, 3 H), 6.18 (dd, J = 6.0, 1.8 Hz, 1 H), 5.45 – 5.40 (m, 1 H), 5.24 – 5.20 (m, 1 H), 4.35 (s, 2 H), 3.67 – 3.63 (m, 1 H), 3.34 – 3.32 (s, 5 H), 3.14 – 3.12 (m, 1 H), 2.58 (ddd, J = 13.7, 10.4, 6.1 Hz, 1 H), 2.45 – 2.33 (m, 3 H), 2.26 – 2.22 (m, 1 H), 2.07 (td, J = 11.0, 7.2 Hz, 1 H), 1.98 – 1.90 (m, 2 H), 1.63 – 1.55 (m, 4 H), 1.45 – 1.40 (m, 2 H), 0.97 (s, 9 H), 0.07 (s, 3 H), 0.02 (s, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 194.84, 160.43, 159.76, 143.51, 139.48, 135.23, 132.70, 131.97, 131.37, 130.98 (q, J = 32.3 Hz), 130.95, 129.39, 129.24, 125.49, 125.34 (q, J = 3.8 Hz), 125.09 (q, J = 276.3 Hz), 123.04 (q, J = 3.5 Hz), 114.13, 72.87, 71.28, 69.97, 54.82, 43.49, 39.14, 37.37, 31.62, 30.94, 29.96, 27.58, 26.75, 26.05, 18.29, -4.10, -4.47 ppm; HR-MS (ESI-TOF): calcd for $C_{38}H_{51}O_4F_3SiNa$ [M+Na]: 679.3401, found: 679.3398.

S47

(4*S*,5*E*)-5-{(3*S*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-5-[3-(trifluoromethyl)phenyl]pentylidene}-4-[(2*Z*)-7-hydroxyhept-2-en-1-yl]cyclopent-2-en-1-one (101): To a vigorously stirred solution



of dienone **100** (180 mg, 0.270 mmol, 1.0 equiv) in a mixture of $CH_2Cl_2:H_2O$ (20:1, 3 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (120 mg, 0.540 mmol, 2.0 equiv). After stirring at this temperature for 45 min, the reaction mixture was diluted

with Et_2O (30 mL), filtered through Celite, washed with Et_2O , and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 2:1) yielded pure title compound (**101**, 125 mg, 0.232 mmol, 86% yield) as a colorless oil.

101: $R_f = 0.10$ (hexanes: EtOAc, 4:1); $[\alpha]_D^{25} = +126.1$ (c = 0.7 in C_6H_6); IR (film): $v_{max} = 3421, 2951, 2935, 2860, 1722, 1650, 1462, 1329, 1256, 1163, 1073, 1033, 836 cm⁻¹; ¹H-NMR (600 MHz, <math>C_6D_6$) δ 7.43 (s, 1 H), 7.26 (d, J = 7.7 Hz, 1 H), 7.02 (d, J = 7.7 Hz, 1 H), 6.98 (dd, J = 6.1, 2.5 Hz, 1 H), 6.95 (t, J = 7.7 Hz, 1 H), 6.78 (t, J = 7.8 Hz, 1 H), 6.20 (dd, J = 6.0, 1.8 Hz, 1 H), 5.44 – 5.19 (m, 1 H), 3.70 – 3.66 (m, 1 H), 3.42 (t, J = 6.3 Hz, 2 H), 3.14 – 3.12 (m, 1 H), 2.60 (ddd, J = 13.7, 10.4, 6.1 Hz, 1 H), 2.43 (ddt, J = 9.9, 7.3, 5.3 Hz, 2 H), 2.36 (dt, J = 14.8, 6.3 Hz, 1 H), 2.26 (ddd, J = 14.9, 8.5, 6.4 Hz, 1 H), 2.06 (dt, J = 14.9, 8.5 Hz, 1 H), 1.96 – 1.84 (m, 2 H), 1.67 – 1.54 (m, 2 H), 1.44 – 1.39 (m, 2 H), 1.35 – 1.30 (m, 2 H), 0.96 (s, 9 H), 0.07 (s, 3 H), 0.02 (s, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 195.18, 160.76, 143.53, 139.49, 135.16, 132.75, 132.01, 131.21, 130.98 (q, J = 32.3 Hz), 129.25, 125.41, 125.34 (q, J = 3.8 Hz), 125.09 (q, J = 276.3 Hz), 123.04 (q, J = 3.9 Hz), 71.32, 62.40, 43.55, 39.15, 37.42, 32.70, 31.65, 30.90, 27.49, 26.22, 26.09, 18.30, -4.11, -4.47 ppm; HR-MS (ESI-TOF): calcd for $C_{30}H_{43}F_3O_3SiNa$ [M+Na]⁺: 559.2826, found: 559.2819.

(5Z)-7-[(1S,5E)-5-{(3S)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-5-[3-(trifluoromethyl)phenyl]pentylidene}-4-oxocyclopent-2-en-1-yl]hept-5-enoic acid (103): To a vigorously stirred solution



of hydroxy dienone **101** (125 mg, 0.232 mmol, 1.0 equiv) in CH₂Cl₂ (2 mL) at 25 °C was added in one portion pyridinium chlorochromate (106 mg, 0.464 mmol, 2.0 equiv). After stirring for 2 h, the reaction mixture was diluted with Et₂O (30 mL), filtered through Celite, washed

with Et₂O, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column

chromatography (SiO₂, hexanes:EtOAc, 5:1) yielded aldehyde (**102**, 101 mg, 0.187 mmol, 82 % yield) as a colorless oil.

To a vigorously stirred solution of aldehyde dienone **102** (100 mg, 0.187 mmol, 1.0 equiv) in *t*-BuOH (2 mL) at 25 °C were sequentially dropwise added 2-methyl-2-butene (0.400 mL, 3.73 mmol, 20 equiv), a solution of NaH₂PO₄ (0.3 M solution in H₂O, 1.87 mL, 0.560 mmol, 3.0 equiv) and a solution of NaClO₂ (80 %, 63.0 mg, 0.560 µmol, 3.0 equiv) in H₂O (1.5 mL). After stirring for 30 min, the reaction mixture was diluted with a solution of NaH₂PO₄ (4.0 g) in H₂O (80 mL) and extracted with EtOAc (5 × 40 mL). The combined organic extracts were washed with sat. brine (50 mL), dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 1:1) yielded pure title compound (**103**, 94.6 mg, 0.175 mmol, 72 % yield for the two steps) as a colorless oil. **103:** R_f=0.57 (hexanes:EtOAc, 1:4); $[\alpha]_{D}^{25} = +95.3$ (*c*=0.5 in C₆H₆); IR (film): v_{max}=3010, 2952,

103: $R_f = 0.57$ (nexanes:EtOAc, 1:4); $[a]_D^{-} = +95.3$ (c = 0.5 in C₆H₆); IR (nim): $v_{max} = 3010, 2952, 2934, 2859, 1706, 1657, 1472, 1455, 1389, 1328, 1256, 1200, 1163, 1073, 1033, 836, 776 cm⁻¹; ¹H-NMR (600 MHz, C₆D₆) <math>\delta$ 7.44 (s, 1 H), 7.26 (d, J = 7.7 Hz, 1 H), 7.02 (d, J = 7.7 Hz, 1 H), 6.95 – 6.93 (m, 2 H), 6.79 (t, J = 7.5 Hz, 1 H), 6.22 (dd, J = 6.0, 1.8 Hz, 1 H), 5.28 – 5.23 (m, 1 H), 5.22 – 5.17 (m, 1 H), 3.66 – 3.60 (m, 1 H), 3.12 – 3.09 (m, 1 H), 2.61 (ddd, J = 13.8, 10.5, 6.0 Hz, 1 H), 2.45 – 2.33 (m, 3 H), 2.26 (ddd, J = 14.9, 8.5, 6.5 Hz, 1 H), 2.08 (t, J = 7.2 Hz, 2 H), 2.01 (dt, J = 14.1, 8.4 Hz, 1 H), 1.88 – 1.81 (m, 2 H), 1.67 – 1.56 (m, 2 H), 1.50 (quint, J = 7.3 Hz, 2 H), 0.97 (s, 9 H), 0.08 (s, 3 H), 0.03 (s, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 195.06, 178.54, 160.52, 143.49, 139.41, 135.22, 131.99, 131.46, 131.21, 130.98 (q, J = 32.3 Hz), 129.24, 126.33, 125.36 (q, J = 3.8 Hz), 125.09 (q, J = 276.3 Hz), 123.06 (q, J = 3.5 Hz), 71.43, 43.38, 39.13, 37.41, 33.21, 31.66, 30.82, 26.76, 26.08, 24.62, 18.31, -4.13, -4.49 ppm; HR-MS (ESI-TOF): calcd for C₃₀H₄₁F₃O₄SiNa [M+Na]⁺: 573.2618, found: 573.2617.

(5*Z*)-7-[(1*S*,5*E*)-5-{(3*S*)-3-Hydroxy-5-[3-(trifluoromethyl)phenyl]pentylidene}-4-oxocyclopent-2-en-1-yl]hept-5-enoic acid (25): To a stirred solution of 15-*t*-butyldimethylsilyl ether 103



(90 mg, 0.16 mmol, 1.0 equiv) in MeCN (1.5 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 650 μ L, ca. 16 mmol, ca. 100 equiv) in MeCN (1.5 mL). After stirring for 45 min at this temperature, the reaction mixture was quenched with sat. brine (10 mL) and extracted

with EtOAc (5 \times 50 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and

concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 1:4) yielded pure title compound (25, 57 mg, 0.14 mmol, 84 % yield) as a colorless oil.

25: $R_f = 0.20$ (hexanes: EtOAc, 1:4); $[\alpha]_D^{25} = +108.9$ (c = 0.3 in C_6H_6); IR (film): $v_{max} = 3397$, 3011 cm^{-1} ; ¹H-NMR (600 MHz, C₆D₆) δ 7.47 (s, 1 H), 7.27 (d, J=7.8 Hz, 1 H), 7.07 (d, J=7.7 Hz, 1) 1 H), 7.00 (dd, J = 5.9, 2.7 Hz, 1 H), 6.97 (t, J = 7.6 Hz, 1 H), 6.77 (t, J = 7.5 Hz, 1 H), 6.22 (dd, J=6.0, 1.7 Hz, 1 H), 5.33 – 5.26 (m, 1 H), 5.24 – 5.19 (m, 1 H), 3.63 – 3.58 (m, 1 H), 3.09 – 3.08 (m, 1 H), 2.75 – 2.70 (m, 1 H), 2.55 – 2.48 (m, 2 H), 2.36 (dt, J = 14.9, 7.4 Hz, 1 H), 2.20 – 2.10 (m, 3 H), 1.94 (q, J = 7.4 Hz, 3 H), 1.68 – 1.60 (m, 1 H), 1.59 – 1.47 (m, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 196.12, 177.58, 161.60, 143.46, 139.87, 135.02, 132.22, 132.06, 131.62, 130.92 (q, J = 32.3 Hz), 129.17, 126.49, 125.54 (q, J = 3.8 Hz), 125.09 (q, J = 276.3 Hz), 123.00 (q, J=3.5 Hz), 70.37, 43.74, 38.56, 37.74, 33.00, 32.00, 30.70, 26.63, 24.66 ppm; HR-MS (ESI-TOF): calcd for C₂₄H₂₇F₃O₄Na [M+Na]⁺: 459.1754, found: 459.1765.

Methyl (5Z)-7-[(1S,5E)-5-{(3S)-3-hydroxy-5-[3-(trifluoromethyl)phenyl]pentylidene}-4-oxocyclopent-2-en-1-yl]hept-5-enoate (26): To a stirred solution of Δ^{12} -PGJ₃ analog 25 (13 mg,



30 µmol, 1.0 equiv) in C₆H₆:MeOH (3:2, 2.0 mL) at 25 °C was dropwise added a solution of trimethylsilyl diazomethane (2 M in Et₂O, 30 µL, 60 µmol, 2.0 equiv) (yellow color persists). After stirring for 30 min, the reaction mixture was concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc,

2:1 \rightarrow 3:2) yielded pure title compound (26, 12 mg, 26 µmol, 86 % yield) as a colorless oil.

26: $R_f = 0.51$ (hexanes: EtOAc, 1:1); $[\alpha]_D^{25} = +103.8$ (c = 0.3 in C_6H_6); IR (film): $v_{max} = 3444$, 3007, 2952, 2923, 1735, 1698, 1649, 1656, 1456, 1328 1121, 1072, 1015, 799 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6 δ 7.41 (s, 1 H), 7.26 (d, J=7.7 Hz, 1 H), 6.99 (d, J=7.7 Hz, 1 H), 6.94 - 6.92 (m, 2 H), 6.73 (t, J=7.5 Hz, 1 H), 6.20 (dd, J=6.0, 1.8 Hz, 1 H), 5.27 (dt, J=10.8, 7.3 Hz, 1 H), 5.19-5.15 (m,1 H), 3.38 – 3.33 (m, 4 H), 3.07 (ddt, J=8.2, 3.8, 1.9 Hz, 1 H), 2.61 (ddd, J=14.5, 9.7, 5.4 Hz, 1 H), 2.44 - 2.38 (m, 2 H), 2.19 (dt, J = 14.9, 7.5 Hz, 1 H), 2.08 - 1.97 (m, 4 H), 1.87 - 1.84 (m, 2 H), 1.66 (d, J = 1.7 Hz, 1 H), 1.54 – 1.43 (m, 4 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 195.13, 173.52, 160.59, 143.54, 139.77, 135.26, 132.16, 131.58, 131.29, 130.93 (g, J=32.6 Hz), 129.11, 126.23, 125.46 (q, J=3.8 Hz), 125.09 (q, J=276.3 Hz), 122.99 (q, J=3.8 Hz), 69.85, 51.13, 43.38,

38.77, 37.90, 33.24, 31.95, 30.55, 26.89, 24.92. ppm; HR-MS (ESI-TOF): calcd for C₂₅H₂₉F₃O₄Na [M+Na]⁺: 473.1910, found: 473.1908.

(1*E*,3*S*,9*Z*,11a*S*)-3-{2-[3-(trifluoromethyl)phenyl]ethyl}-2,6,7,8,11,11a-hexahydro-3*H*-cyclopenta[*e*]oxacyclotridecine-5,14-dione (27): To a stirred solution of 2-methyl-6-nitrobenzoic

anhydride (12 mg, 34 µmol, 1.4 equiv) and 4-dimethylaminopyridine (11 mg, 93 µmol, 6.0 equiv) in CH₂Cl₂ (20 mL) was added a solution of Δ^{12} -PGJ₃ ÇF₃ analog 25 (10 mg, 23 µmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at 25 °C dropwise via syringe pump over 6 h. After stirring for an additional 12 h, the reaction mixture was washed sequentially with sat. aq. NaHCO₃-solution (3 mL), a and sat. brine (3 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 3:2) yielded pure title compound (27, 6.1 mg, 14 µmol, 61 % yield) as a colorless oil. **27:** $R_f = 0.35$ (hexanes: EtOAc, 3:1); $[\alpha]_D^{25} = +33.0$ (c = 0.4 in C_6H_6); IR (film): $v_{max} = 3010$, 2961, 2927, 2855, 1727, 1704, 1655, 1581, 1456, 1440, 1239, 1151, 1024 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6 δ 7.33 (s, 1 H), 7.26 (d, J=7.3 Hz, 1 H), 6.95 – 6.90 (m, 2 H), 6.77 (dd, J=6.1, 2.6 Hz, 1 H), 6.59 (dd, J=11.4, 4.6 Hz, 1 H), 6.19 (dd, J=6.0, 1.9 Hz, 1 H), 5.18 (td, J=10.3, 5.8 Hz, 1 H), 5.12 -5.07 (m, 1 H), 5.06 - 5.01 (m, 1 H), 3.21 - 3.18 (m, 1 H), 2.40 (ddd, J = 14.6, 9.3, 5.7 Hz, 1 H), 2.36 - 2.25 (m, 3 H), 2.17 (ddd, J = 15.1, 11.4, 9.5 Hz, 1 H), 2.13 - 2.07 (m, 2 H), 1.97 - 1.89 (m, 2 H), 1.79 (dq, J = 13.8, 6.8 Hz, 1 H), 1.67 – 1.60 (m, 1 H), 1.39 – 1.24 (m, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ ¹³C-NMR (151 MHz, C₆D₆) δ 194.64, 172.44, 159.60, 142.61, 140.45, 135.59, 132.04, 131.79, 130.94 (q, J = 32.6 Hz), 130.33, 129.19, 125.47, 125.46 (q, J = 3.8 Hz), 125.09 (q, J = 276.3 Hz), 122.96 (q, J = 3.6 Hz), 72.52, 43.42, 35.63, 34.14, 32.66, 31.84, 28.40, 26.04, 24.56 ppm; HR-MS (ESI-TOF): calcd for C₂₄H₂₆F₃O₃ [M+H]⁺: 441.1648, found: 441.1634.

Synthesis of Δ^{12} -PGJ₃ Analog **28**, its Methyl Ester **29** and Lactone **30**.

(3S)-1-[(4-Methoxybenzyl)oxy]-6-(trimethylsilyl)hex-5-yn-3-ol (105): To a stirred solution of TMS-acetylene (5.30 mL, 37.5 mmol, 1.5 equiv) in THF (50 mL) at -78 °C was dropwise added *n*-butyl lithium (1.6 M in hexane, 20.3 mL, 32.5 mmol, 1.3 equiv) and the reaction mixture was stirred for 30 min at -78 °C and then for 1 h at -40 °C. A solution of epoxide 104⁵ (5.20 g, 25.0 mmol, 1.0 equiv) in THF (15 mL) was added

all at once followed by dropwise addition of $BF_3 \cdot Et_2O$ (4.01 mL, 32.5 mmol, 1.3 equiv) at -78 °C. After stirring at the same temperature for an additional 2 h, the reaction mixture was partitioned between sat. aq. NH₄Cl-solution (100 mL) and EtOAc (200 mL). The organic layer was separated and washed sequentially with H₂O (100 mL) and brine (100 mL), and the combined aqueous layers were re-extracted with EtOAc (2 × 100 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 4:1) gave pure title compound (**105**, 6.73 g, 22.0 mmol, 88 % yield) as a colorless oil.

105: $R_f = 0.57$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +4.4$ (c = 1.0, C_6H_6); IR (film): $v_{max} = 3446$, 2956, 2933, 2861, 2175, 1612, 1514, 1248, 1096, 1035, 842 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.26 – 7.22 (m, 2 H), 6.90 – 6.85 (m, 2 H), 4.45 (s, 2 H), 3.94 (dtd, J = 9.2, 6.3, 3.1 Hz, 1 H), 3.80 (s, 3 H), 3.71 (ddd, J = 9.3, 6.2, 4.5 Hz, 1 H), 3.63 (ddd, J = 9.4, 7.8, 4.3 Hz, 1 H), 2.49 – 2.37 (m, 2 H), 1.90 (dddd, J = 14.0, 6.2, 4.3, 3.1 Hz, 1 H), 1.85 – 1.77 (m, 1 H), 1.14 (br s, 1 H), 0.15 (s, 9 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 159.43, 130.13, 129.46, 114.00, 103.51, 87.21, 73.10, 69.71, 68.44, 55.42, 35.44, 28.72, 0.23 ppm; HR-MS (ESI-TOF): calcd for C₁₇H₂₇O₃Si [M+H]⁺: 307.1724, found: 307.1722.

(3S)-1-[(4-Methoxybenzyl)oxy]hex-5-yn-3-ol (106): To a stirred solution of alcohol 105 (6.10 g, $PMBO_{106}$ 20.0 mmol, 1.0 equiv) in THF (80 mL) at 0 °C was added dropwise tetra *n*-butylammonium fluoride (1 M in THF, 24.0 mL, 24.0 mmol, 1.2 equiv). After warming the reaction mixture to 25 °C, stirring was continued for 2 h. The brown solution was then quenched by addition of sat. aq. NH₄Cl-solution (50 mL) and diluted with EtOAc (100 mL). The phases were separated, the aqueous layer was extracted with EtOAc (3 × 100 mL), and the combined organic extracts were washed with sat. brine (20 mL), dried (MgSO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 5:2) yielded pure title compound (106, 4.40 g, 18.8 mmol, 94 %) as a colorless oil, which was taken to the next step without further purification.

106: $R_f = 0.34$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +8.0$ (c = 1.0, C_6H_6); IR (film): $v_{max} = 3426$, 3291, 2920, 2861, 1612, 1513, 1247, 1174, 1085, 1033, 820 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 7.16 – 7.09 (m, 2 H), 6.79 – 6.74 (m, 2 H), 4.19 – 4.15 (m, 2 H), 3.88 (dtd, J = 9.3, 6.2, 3.4 Hz, 1 H), 3.42 (ddd, J = 9.3, 6.3, 4.7 Hz, 1 H), 3.32 (ddd, J = 9.3, 7.5, 4.7 Hz, 1 H), 3.30 (s, 3 H), 2.76 (s, 1 H), 2.28

(ddd, J = 16.6, 5.8, 2.7 Hz, 1 H), 2.20 (ddd, J = 16.6, 6.6, 2.7 Hz, 1 H), 1.76 – 1.66 (m, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 159.83, 130.67, 129.45, 114.16, 81.44, 73.00, 70.72, 69.52, 68.26, 54.80, 35.89, 27.61 ppm.

(3S,5Z,8Z)-1-[(4-Methoxybenzyl)oxy]undeca-5,8-dien-3-ol (109): To a solution of terminal alkyne 106 (1.50 g, 6.42 mmol, 1.0 equiv.) in PMBO_ 109 ōн N,N-dimethylformamide (7 mL) was added sequentially 1-bromo-2-pentyne (0.790 mL, 7.72 mmol, 1.2 equiv.), K₂CO₃ (1.15 g, 8.36 mmol, 1.3 equiv.), CuI (1.59 g, 8.36 mmol, 1.3 equiv.), and NaI (1.25 g, 8.36 mmol, 1.3 equiv.). The resulting heterogeneous mixture was sealed tightly in a pressure tube and vigorously stirred in the dark for 15 h. The reaction mixture was then diluted with H₂O (3 mL) and Et₂O (3 mL), filtered through Celite (Et₂O), and concentrated under reduced pressure. The crude residue was resuspended in Et₂O (10 mL) and washed sequentially with sat. aq. NH₄Cl solution (10 mL) and brine (10 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The unstable (light sensitive) skipped divne 108 was directly carried to the next step without further purification.

To a stirred suspension of Ni(OAc)₂·4H₂O (478 mg, 1.92 mmol, 0.32 equiv) in EtOH (50 mL) under a hydrogen atmosphere was added NaBH₄ (172 mg, 4.56 mmol, 0.76 equiv) as a solution in EtOH (10 mL). The flask headspace was evacuated and refilled with H₂ three times. After the black suspension was stirred for 10 min at 25 °C, a solution of 1,2-ethylenediamine (1.44 mL, 21.6 mmol, 3.6 equiv) in EtOH (20 mL) was added, and the flask headspace was evacuated and refilled with H₂ three times. After stirring for 20 min, a solution of above prepared skipped diyne **108** (1.80 g, 6.00 mmol, 1.0 equiv) in EtOH (20 mL) was added, and the headspace was evacuated again and refilled with H₂ three more times. The reaction flask was then shielded from light with aluminum foil and stirred at 25 °C for 18 h. The H₂ atmosphere was removed, and the solution was concentrated under reduced pressure. The crude material was redissolved in EtOAc (200 mL) and washed sequentially with saturated aqueous NH₄Cl-solution (30 mL) and brine (30 mL). The aqueous layers were re-extracted with EtOAc (2 × 100 mL) and the combined organic layers were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 19:1) gave pure title compound (**109**, 1.50 g, 4.95 mmol, 77 % yield) as a colorless oil.

109: $R_f = 0.54$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +5.1$ (c = 1.0, C_6H_6); IR (film): $v_{max} = 3425$, 3008, 2960, 2933, 2861, 1612, 1512, 1302, 1246, 1173, 1084, 1034, 820 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 7.15 (d, J = 5.9 Hz, 2 H), 6.79 – 6.75 (m, 2 H), 5.55 – 5.47 (m, 2 H), 5.44 – 5.36 (m, 2 H), 4.25 – 4.21 (m, 2 H), 3.82 (dtt, J = 9.1, 6.1, 3.0 Hz, 1 H), 3.49 (ddd, J = 9.2, 6.2, 4.8 Hz, 1 H), 3.42 (s, 1 H), 3.40 (ddd, J = 9.3, 7.7, 4.7 Hz, 1 H), 3.30 (s, 3 H), 2.80 (t, J = 5.5 Hz, 2 H), 2.64 (d, J = 3.1 Hz, 1 H), 2.35 – 2.29 (m, 1 H), 2.22 (ddd, J = 13.8, 6.2, 5.1 Hz, 1 H), 2.04 – 1.96 (m, 1 H), 1.69 (dddd, J = 13.7, 8.8, 7.7, 4.8 Hz, 1 H), 1.62 (dddd, J = 14.1, 6.2, 4.6, 3.0 Hz, 1 H), 0.90 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 159.82, 132.09, 130.80, 130.62, 129.46, 127.58, 126.42, 114.17, 73.06, 70.82, 68.75, 54.80, 36.65, 35.96, 26.15, 20.95, 14.50 ppm; HR-MS (ESI-TOF): calcd for $C_{19}H_{29}O_3$ [M+H]⁺: 305.2111, found: 305.2110.

tert-Butyl({(3S,5Z,8Z)-1-[(4-methoxybenzyl)oxy]undeca-5,8-dien-3-yl}oxy)dimethylsilane

(110): To a stirred solution of alcohol 109 (1.50 g, 4.93 mmol, 1.0 equiv) in CH₂Cl₂ (15 mL) at $PMBO \xrightarrow{T}{OTBS} 110$ $O^{\circ}C$ was added imidazole (0.960 g, 14.8 mmol, 3.0 equiv) and TBSCl (0.980 g, 7.40 mmol, 1.5 equiv). The reaction mixture was warmed to 25 °C and stirred for 12 h. The resulting mixture was then quenched by addition of sat. aq. NH₄Cl-solution (50 mL) and stirred vigorously for 30 min. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 50 mL). The combined organic extracts were washed sequentially with H₂O (2 × 100 mL), brine (100 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 19:1) gave pure title compound (110, 1.90 g, 4.55 mmol, 91 % yield) as a colorless oil.

110: $R_f = 0.43$ (hexanes: Et₂O, 19:1); $[\alpha]_D^{25} = +9.0$ (c = 1.0, C_6H_6); IR (film): $v_{max} = 3009$, 2955, 2930, 2930, 2856, 1742, 1613, 1513, 1248, 1093, 1039, 835, 774 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.26 - 7.25 (m, 2 H), 6.88 - 6.86 (m, 2 H), 5.46 - 5.35 (m, 3 H), 5.33 - 5.25 (m, 1 H), 4.44 (d, J = 11.5 Hz, 1 H), 4.39 (d, J = 11.4 Hz, 1 H), 3.91 - 3.84 (m, 1 H), 3.80 (s, 3 H), 3.54 - 3.48 (m, 2 H), 2.79 - 2.74 (m, 1 H), 2.29 - 2.18 (m, 2 H), 2.10 - 1.99 (m, 2 H), 1.78 (dtd, J = 14.2, 7.2, 4.3 Hz, 1 H), 1.72 - 1.64 (m, 1 H), 1.37 - 1.23 (m, 1 H), 0.97 (t, J = 7.5 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 159.25, 132.08, 130.83, 130.01, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 69.39, 67.00, 55.42, 36.94, 35.73, 26.03, 25.88, 20.71, 129.42, 127.26, 125.85, 113.89, 72.76, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 120.81, 12

18.23, 14.42, -4.18, -4.59 ppm; HR-MS (ESI-TOF): calcd for C₂₅H₄₃O₃Si [M+H]⁺: 419.2976, found: 419.2974.

(3S,5Z,8Z)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}undeca-5,8-dien-1-ol (111): To a vigorously $HO_{\frac{1}{OTBS}}$ 111 stirred solution of skipped diene 110 (1.90 g, 4.54 mmol, 1.0 equiv) in CH₂Cl₂:H₂O (10:1, 20 mL) at 0 °C was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.55 g, 6.81 mmol, 1.5 equiv) at 0 °C. The reaction mixture was slowly warmed to 25 °C and stirred for an additional 1.5 h before being quenched by the addition of sat. aq. NaHCO₃-solution (25 mL) and the mixture was stirred vigorously for 30 min. The layers were separated and the aqueous layer was extracted with Et₂O (3 × 200 mL). The combined organic layers were dried (Na₂SO₄) and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 9:1) gave pure title compound (111, 885 mg, 2.96 mmol, 66 % yield) as a colorless oil.

111: $R_f = 0.40$ (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = +31.5$ (c = 1.0, CHCl₃); IR (film): $v_{max} = 3350$, 3011, 2956, 2929, 2857, 1472, 1463, 1361, 1254, 1091, 1067, 834, 774 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 5.47 – 5.34 (m, 3 H), 5.31 – 5.27 (m, 1 H), 3.98 – 3.94 (m, 1 H), 3.83 (ddd, J = 10.7, 8.3, 4.3 Hz, 1 H), 3.72 (dt, J = 10.7, 5.4 Hz, 1 H), 2.83 – 2.74 (m, 1 H), 2.36 – 2.28 (m, 2 H), 2.23 (br s, 1 H), 2.07 (quint, J = 7.5 Hz, 2 H), 1.81 (ddt, J = 14.2, 8.6, 4.3 Hz, 1 H), 1.65 (dtd, J = 14.2, 6.4, 4.3 Hz, 1 H), 0.97 (t, J = 7.5 Hz, 3 H), 0.90 (s, 9 H), 0.104 (s, 3 H), 0.097 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 132.28, 130.46, 126.98, 125.36, 71.87, 60.49, 37.79, 35.11, 25.97, 25.90, 20.74, 18.13, 14.40, -4.21, -4.67 ppm; HR-MS (ESI-TOF): calcd for C₁₇H₃₄O₂SiH⁺ [M+H]⁺: 299.2401, found: 299.2410.

 $(3S,5Z,8Z)-3-\{[tert-Butyl(dimethyl)silyl]oxy\}undeca-5,8-dienal (112): To a solution of primary$ alcohol 111 (127 mg, 0.426 mmol, 1.0 equiv) in CH₂Cl₂ (4.5 mL)at 0 °C was added Dess-Martin periodinane (271 mg, 0.639 mmol,

1.5 equiv) in one portion. The resulting mixture was allowed to warm to 25 °C and stirred for 90 min. The reaction was quenched sequentially by addition of sat. aq. NaHCO₃ (4 mL) and sat. aq. Na₂S₂O₃ (4 mL) and stirred for 10 min. The layers were separated, and the aq. phase was extracted with CH₂Cl₂ (10 mL). The combined organic extracts were dried (MgSO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc,

 $98:2 \rightarrow 95:5 \rightarrow 93:7$) yielded the title aldehyde **112** (101 mg, 0.341 mmol, 80% yield) as a colorless oil.

112: $R_f = 0.50$ (hexanes:EtOAc, 9:1); $[\alpha]_D^{25} = +23.7$ (c = 1.0, CHCl₃); IR (film): $v_{max} = 3012$, 2957, 2930, 2857, 1727, 1472, 1463, 1255, 1101, 836, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 9.80 (br s, 1 H), 5.51 – 5.47 (m, 1 H), 5.42 – 5.36 (m, 2 H), 5.30 – 5.26 (m, 1 H), 4.25 (quint, J = 5.8 Hz, 1 H), 2.81 – 2.73 (m, 2 H), 2.54 – 2.49 (m, 2 H), 2.38 – 2.27 (m, 2 H), 2.06 (quint, J = 7.5 Hz, 2 H), 0.97 (t, J = 7.5 Hz, 3 H), 0.87 (s, 9 H), 0.09 (s, 3 H), 0.06 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 202.27, 132.39, 131.27, 126.78, 124.66, 68.23, 50.63, 35.80, 25.89, 25.87, 20.75, 18.13, 14.39, -4.22, -4.67 ppm; HR-MS (ESI-TOF): calcd for C₁₇H₃₃O₂Si [M+H]⁺: 297.2244, found:297.2236.

{4-[(4-Methoxybenzyl)oxy]butyl}(triphenyl)phosphonium iodide (115): To a stirred solution of 1-[(4-iodobutoxy)methyl]-4-methoxybenzene⁶ (2.10 g, 6.60 mmol, IPh₃P ОРМВ 1.0 equiv) in benzene (50 mL) at 25 °C was added triphenylphosphine 115 (8.60 g, 33.0 mmol, 5.0 equiv). The reaction mixture was heated to reflux for 18 h, allowed to cool to 25 °C, and the benzene layer was decanted from the solidified crude product. Flash column chromatography (SiO₂, CH₂Cl₂:MeOH, 98:2 \rightarrow 95:5) yielded the title compound (115, 3.06 g, 5.25 mmol, 81 % yield) as a colorless amorphous solid along with some traces of IPh₃PPMB. **115:** $R_f = 0.40$ (CH₂Cl₂:MeOH, 19:1); FT-IR (neat): $v_{max} = 3055$, 3010, 2932, 2861, 2793, 2187, 1611, 1586, 1511, 1437, 1302, 1246, 1178, 1111, 1028, 915, 718 cm⁻¹; ¹H-NMR (600 MHz, $CDCl_3$) δ 7.82 - 7.74 (m, 10 H), 7.69 - 7.62 (m, 5 H), 7.17 (d, J=8.6 Hz, 2 H), 6.81 (d, J=8.6 Hz, 2 H), 7.81 (d, J=8.6 Hz, 2 Hz), 7.81 (d, J=8.6 Hz, 2 Hz), 7.81 (d, J=8.6 Hz), 7.81 (d, J=8.6 2 H), 4.39 (s, 2 H), 3.78 (s, 3 H), 3.74 – 3.67 (m, 2 H), 3.58 (t, J = 5.7 Hz, 2 H), 1.99 (quint, J = 6.4 Hz, 2 H), 1.82 - 1.72 (m, 2 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 159.24, 135.13 (d, J=2.9 Hz), 133.86 (d, J=10.0 Hz), 130.60 (d, J=12.5 Hz), 129.51, 118.34 (d, J=86.1 Hz), 113.86, 72.56, 68.57, 55.46, 29.63 (d, J = 16.4 Hz), 22.49 (d, J = 50.0 Hz), 19.74 (d, J = 4.1 Hz) ppm; ³¹P-NMR (162 MHz, CDCl₃) δ 24.81 ppm; HR-MS (ESI) calcd for C₃₀H₃₂O₂P⁺ [M–I]⁺: 455.2134, found: 455.2138.

(4*R*)-4-{(2*Z*)-6-[(4-Methoxybenzyl)oxy]hex-2-en-1-yl}cyclopent-2-en-1-ol (117): To a stirred solution of *t*-butyldimethylsilyl-alcohol 113 (660 mg, 2.44 mmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at -78 °C was dropwise added diisobutylaluminum hydride (1 M in CH₂Cl₂, 2.60 mL, 2.60 mmol, 1.1 equiv). After stirring for 45 min, the clear solution was quenched with H₂O (900 μ L, 50.0 mmol, 20 equiv), diluted with Et₂O (5.6 mL) and allowed to warm to 25 °C. Under vigorous stirring was added NaF (1.00 g, 24.0 mmol, 10 equiv) and the resulting mixture was stirred for an additional 30 min before it was filtered through Celite, washed with Et₂O, and concentrated under reduced pressure. Flash column chromatography (SiO₂, pentane:Et₂O, 10:1) yielded the corresponding aldehyde (**114**, 550 mg, 2.29 mmol), which was taken to the next step without further purification.

To a stirred solution of phosphonium iodide **115** (2.00 g, 3.40 mmol, 1.5 equiv) in THF (23 mL) at 0 °C was added dropwise sodium bis(trimethylsilyl)amide (1 M in THF, 4.60 mL, 4.60 mmol, 2.0 equiv). After stirring for 30 min at this temperature, the resulting bright orange solution was cooled to -78 °C, and the aldehyde obtained above (550 mg, 2.29 mmol, 1.0 equiv) in THF (1.5 mL) was added dropwise. After stirring at this temperature for 1 h, the reaction mixture was allowed to warm to 25 °C over 2 h and stirred for an additional 12 h. The reaction was then quenched by addition of sat. aq. NH₄Cl solution (20 mL) and extracted with hexanes (4 × 20 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, pentane:Et₂O, 25:1 \rightarrow 8:1) yielded the alkene **116** along with a small impurity as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of the obtained diene (700 mg, 1.68 mmol, 1.0 equiv) in THF (20 mL) at 0 °C was added dropwise tetra-*n*-butylammonium fluoride (1 M in THF, 2.02 mL, 2.02 mmol, 1.2 equiv). After warming the reaction mixture to 25 °C, stirring was continued for 3 h. The brown-colored reaction was then quenched by addition of sat. aq. NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The phases were separated, the aq. layer was extracted with EtOAc (3 × 20 mL), and the combined organic extracts were washed with brine (20 mL), dried (MgSO₄), filtered, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 5:2) yielded the pure title compound (**117**, 500 mg, 1.65 mmol, 68 % for the three steps, dr > 20:1 by ¹H-NMR analysis) as a colorless oil.

117: $R_f = 0.32$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{25} = +17.2$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 3391$, 3004, 2931, 2853, 1612, 1586, 1512, 1301, 1245, 1172, 1095, 1033, 819, 758 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.26 (d, J = 8.3 Hz, 2 H), 6.89 (d, J = 8.3 Hz, 2 H), 5.88 – 5.83 (m, 1 H), 5.81 – 5.78 (m, 1 H), 5.49 – 5.43 (m, 1 H), 5.43 – 5.36 (m, 1 H), 4.77 (t, J = 5.9 Hz, 1 H), 4.43 (s, 2 H), 3.80 (s, 3 H), 3.44 (t, J = 6.5 Hz, 2 H), 2.63 (quint, J = 7.1 Hz, 1 H), 2.45 (dt, J = 13.7, 7.7 Hz, 1 H),

2.25 - 2.18 (m, 1 H), 2.16 - 2.09 (m, 3 H), 1.80 (br s, 1 H), 1.66 (quint, J = 7.0 Hz, 2 H), 1.26 (dt, J = 13.7, 4.9 Hz, 1 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 159.19, 138.22, 133.59, 130.76, 130.75, 129.34, 128.07, 113.85, 77.29, 72.62, 69.52, 55.36, 44.52, 39.81, 33.66, 29.74, 24.08 ppm; HR-MS (ESI) calcd for C₁₉H₂₆O₃Na [M+Na]⁺: 325.1774, found: 325.1781.

(4*R*)-4-{(2*Z*)-6-[(4-Methoxybenzyl)oxy]hex-2-en-1-yl}cyclopent-2-en-1-one (118): To a

vigorously stirred solution of allylic alcohol **117** (120 mg, 0.397 mmol, 1.0 equiv) in CH₂Cl₂ (3.8 mL) at 25 °C was added in one portion pyridinium chlorochromate (164 mg, 0.754 mmol, 1.9 equiv). After stirring for 2 h, the reaction mixture was diluted with Et₂O (10 mL), filtered through Celite, washed with Et₂O, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 3:1) yielded the pure title compound (**118**, 110 mg, 0.367 mmol, 92 % yield) as a colorless oil.

118: $R_f = 0.59$ (hexanes:EtOAc, 3:2); $[\alpha]_D^{25} = +86.1$ (c = 1.1, CHCl₃); FT-IR (neat): $v_{max} = 3006$, 2934, 2855, 1707, 1612, 1586, 1512, 1302, 1246, 1179, 1097, 1034, 820, 783 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) δ 7.59 (dd, J = 5.7, 2.5 Hz, 1 H), 7.24 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 6.14 (dd, J = 5.7, 2.0 Hz, 1 H), 5.53 – 5.46 (m, 1 H), 5.39 – 5.32 (m, 1 H), 4.41 (s, 2 H), 3.79 (s, 3 H), 3.42 (t, J = 6.4 Hz, 2 H), 3.01 - 2.94 (m, 1 H), 2.49 (dd, J = 18.8, 6.4 Hz, 1 H), 2.32 – 2.25 (m, 1 H), 2.23 – 2.13 (m, 1 H), 2.10 (q, J = 7.3 Hz, 2 H), 1.99 (dd, J = 18.8, 2.2 Hz, 1 H), 1.65 (dt, J = 13.5, 6.6 Hz, 2 H) ppm; ¹³C-NMR (125 MHz, CDCl₃) δ 209.83, 168.00, 159.20, 134.16, 132.03, 130.67, 129.28, 126.17, 113.83, 72.65, 69.34, 55.34, 41.45, 40.56, 31.92, 29.62, 24.08 ppm; HR-MS (ESI) calcd for C₁₉H₂₄O₃Na [M+Na]⁺: 323.1618, found: 323.1614.

(4*S*,5*E*)-5-[(3*S*,5*Z*,8*Z*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}undeca-5,8-dien-1-ylidene]-4-{(2*Z*)-6-[(4-methoxybenzyl)oxy]hex-2-en-1-yl}cyclopent-2-en-1-one (121): To a stirred solution of



diisopropylamine (86 μL, 0.62 mmol, 2.2 equiv in THF (2.5 mL)
at 0 °C was added dropwise *n*-butyl lithium (2.5 M in hexanes, 0.22 mL, 0.56 mmol, 2.0 equiv). After stirring for 20 min at this

temperature, the clear solution was cooled to -78 °C, and a solution of enone **118** (82 mg, 0.27 mmol, 1.0 equiv) in THF (2.5 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 20 min at this temperature, a solution of aldehyde **112** (100 mg, 0.340 mmol, 1.3 equiv) in THF (2.5 mL) was added dropwise, and stirring at this temperature was

continued for an additional 30 min. The reaction was then quenched with sat. aq. NH₄Cl solution (7 mL), diluted with EtOAc (7 mL), and allowed to warm to 25 °C. The phases were separated, the aq. layer was extracted with EtOAc (8 mL), and the combined organic extracts were washed with brine (8 mL), dried (Na₂SO₄), filtered, and concentrated. The crude aldol product (**119**) was filtered through a short column (SiO₂, hexanes:EtOAc, $19:1\rightarrow7:3$) to obtain a mixture of diastereomeric alcohols (83 mg, 0.14 mmol, 52 % yield) as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of aldol product **119** (82 mg, 0.14 mmol, 1.0 equiv) in CH₂Cl₂ (2 mL) at 0 °C was added Et₃N (0.19 mL, 1.4 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (53 μ L, 0.69 mmol, 5.0 equiv). After stirring for 60 min at this temperature, the reaction was quenched with sat. aq. NaHCO₃ solution (4 mL), diluted with CH₂Cl₂ (5 mL), and allowed to warm to 25 °C. The phases were separated, and the organic layer was washed with H₂O (10 mL), dried (Na₂SO₄), filtered, and concentrated. The crude mixture (**120**) was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereomeric mesylates as a colorless oil, which was taken to the next step without further purification.

To a vigorously stirred solution of above mesylate **120** in CH₂Cl₂ (3 mL) at 25 °C was added Al₂O₃ (100 mg, 0.98 mmol, 7.0 equiv). After 2 h and 4 h time intervals two more portions of Al₂O₃ (2 × 100 mg, 2 × 0.98 mmol, 2 × 7.0 equiv) were added and vigorous stirring was continued for a total of 6 h. The resulting suspension was then filtered through Celite, washed with EtOAc, and the so obtained solution was concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 19:1 \rightarrow 9:1 \rightarrow 6:1) yielded pure title compound (**121**, 47 mg, 0.081 mmol, 30 % for the three steps) as a colorless oil.

121: $R_f = 0.60$ (hexanes:EtOAc, 4:1); $[\alpha]_D^{25} = +108.8$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 3009$, 2954, 2931, 2856, 1704, 1656, 1613, 1513, 1462, 1248, 1095, 1038, 835, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.47 (ddd, J = 5.9, 2.4, 0.8 Hz, 1 H), 7.24 (d, J = 8.5 Hz, 2 H), 6.87 (d, J = 8.5 Hz, 2 H), 6.60 (dd, J = 8.5, 6.9 Hz, 1 H), 6.31 (dd, J = 6.0, 1.8 Hz, 1 H), 5.51 – 5.32 (m, 5 H), 5.28 – 5.24 (m, 1 H), 4.41 (s, 2 H), 3.90 (quint, J = 6.0 Hz, 1 H), 3.80 (s, 3 H), 3.46 – 3.41 (m, 3 H), 2.78 – 2.69 (m, 2 H), 2.63 – 2.59 (m, 1 H), 2.45 – 2.39 (m, 2 H), 2.30 – 2.15 (m, 3 H), 2.10 – 2.01 (m, 4 H), 1.64 (quint, J = 7.0 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.39, 161.72, 159.28, 138.95, 134.99,

132.51, 132.25, 132.15, 130.74, 130.66, 129.34, 127.00, 125.64, 125.34, 113.91, 72.74, 71.60, 69.53, 55.42, 43.54, 36.97, 35.39, 30.65, 29.74, 25.99, 25.90, 24.18, 20.74, 18.22, 14.40, -4.39, -4.41 ppm; HR-MS (ESI) calcd for C₃₆H₅₄O₄SiNa [M+Na]⁺: 601.3684, found: 601.3661.

(4*S*,5*E*)-5-[(3*S*,5*Z*,8*Z*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}undeca-5,8-dien-1-ylidene]-4-[(2*Z*)-6-hydroxyhex-2-en-1-yl]cyclopent-2-en-1-one (122): To a vigorously stirred solution of dienone



121 (39 mg, 0.067 mmol, 1.0 equiv) in a mixture of CH₂Cl₂:H₂O (10:1, 1.98 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (23 mg, 0.10 mmol, 1.5 equiv). After

stirring at this temperature for 75 min, an additional portion of 2,3-dichloro-5,6-dicyano-1,4benzoquinone (5.0 mg, 0.022 mmol, 0.2 equiv) was added. After stirring for an additional 20 min, the reaction mixture was diluted with Et₂O (3 mL), filtered through Celite, washed with Et₂O, and concentrated under reduced pressure to a volume of ca. 0.5 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 9:1 \rightarrow 3:1 \rightarrow 3:2) yielded pure title compound (**122**, 20 mg, 0.044 mmol, 66 % yield) as a colorless oil.

122: $R_f = 0.30$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +138.3$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 3444$, 3010, 2955, 2929, 2856, 1701, 1652, 1462, 1254, 1071, 835, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.50 (ddd, J = 6.0, 2.5, 0.8 Hz, 1 H), 6.62 – 6.59 (m, 1 H), 6.33 (dd, J = 6.0, 1.8 Hz, 1 H), 5.53 – 5.35 (m, 5 H), 5.29 – 5.24 (m, 1 H), 3.91 (quint, J = 6.0 Hz, 1 H), 3.64 (t, J = 6.4 Hz, 2 H), 3.48 – 3.44 (m, 1 H), 2.79 – 2.69 (m, 2 H), 2.67 – 2.63 (m, 1 H), 2.47 – 2.42 (m, 2 H), 2.31 – 2.18 (m, 3 H), 2.12 – 2.08 (m, 2 H), 2.04 (quint, J = 7.3 Hz, 2 H), 1.61 (quint, J = 7.1 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H), 0.88 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.37, 161.61, 138.94, 135.07, 132.58, 132.28, 131.99, 130.69, 126.99, 125.87, 125.32, 71.63, 62.47, 43.54, 36.97, 35.42, 32.58, 30.65, 25.99, 25.90, 23.84, 20.74, 18.23, 14.40, -4.38, -4.40 ppm; HR-MS (ESI) calcd for C₂₈H₄₆O₃SiNa [M+Na]⁺: 481.3108, found: 481.3103.

(4Z)-6-{(1S,5E)-5-[(3S,5Z,8Z)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}undeca-5,8-dien-1-ylidene]-4-oxocyclopent-2-en-1-yl}hex-4-enal (123): To a vigorously stirred solution of alcohol 122



(19 mg, 0.041 mmol, 1.0 equiv) in CH_2Cl_2 (1 mL) at 25 °C was added in one portion pyridinium chlorochromate (18 mg, 0.082 mmol, 2.0 equiv). After stirring for 75 min, the reaction mixture was filtered through a short pad of Celite (Et₂O), and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, $19:1\rightarrow 9:1\rightarrow 4:1$) provided the intermediate aldehyde (**123**, 15 mg, 0.033 mmol, 80 % yield) as a colorless oil.

123: $R_f = 0.50$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +136.3$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 3011$, 2957, 2930, 2856, 1726, 1704, 1656, 1255, 1089, 836, 808, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 9.76 (br s, 1 H), 7.48 (dd, J = 6.0, 2.6 Hz, 1 H), 6.61 (t, J = 7.7 Hz, 1 H), 6.34 (dd, J = 6.0, 1.2 Hz, 1 H), 5.49 – 5.36 (m, 5 H), 5.29 – 5.23 (m, 1 H), 3.91 (quint, J = 6.0 Hz, 1 H), 3.48 – 3.46 (m, 1 H), 2.79 – 2.69 (m, 2 H), 2.67 – 2.63 (m, 1 H), 2.50 – 2.46 (m, 2 H), 2.45 – 2.41 (m, 2 H), 2.36 – 2.21 (m, 5 H), 2.04 (quint, J = 7.4 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 201.54, 196.24, 161.34, 138.79, 135.20, 132.70, 132.27, 130.69, 130.26, 126.98, 126.75, 125.29, 71.58, 43.68, 43.32, 36.97, 35.42, 30.60, 25.99, 25.90, 20.74, 20.22, 18.22, 14.40, -4.39, -4.41 ppm; HR-MS (ESI) calcd for C₂₈H₄₄O₃SiNa [M+Na]⁺: 479.2952, found: 479.2935.

(4Z)-6-{(1S,5E)-5-[(3S,5Z,8Z)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}undeca-5,8-dien-1-ylidene]-4-oxocyclopent-2-en-1-yl}hex-4-enoic acid (124): To a vigorously stirred solution of aldehyde



123 (15 mg, 0.033 mmol, 1.0 equiv) in *t*-BuOH (0.8 mL) and H₂O (0.6 mL) at 25 °C were added sequentially 2-methyl-2-butene (35 μ L, 0.33 mmol, 10 equiv), NaH₂PO₄ (7.6 mg, 0.049 mmol, 1.5 equiv) and

NaClO₂ (4.4 mg, 0.049 mmol, 1.5 equiv). After stirring for 30 min, the reaction mixture was diluted with a solution of NaH₂PO₄ (500 mg) in H₂O (10 mL) and extracted with EtOAc (2 × 7 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, CH₂Cl₂:EtOH, 49:1 \rightarrow 19:1) yielded pure title compound (**124**, 15 mg, 0.032 mmol, 97 % yield) as a colorless oil.

124: $R_f = 0.45$ (CH₂Cl₂:EtOH, 19:1); $[\alpha]_D^{25} = +93.4$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 3011$, 2956, 2929, 2856, 1707, 1654, 1462, 1253, 1087, 966, 835, 808, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.48 (ddd, J = 6.0, 2.6, 1.0 Hz, 1 H), 6.61 (t, J = 7.7 Hz, 1 H), 6.34 (dd, J = 6.0, 1.8 Hz, 1 H), 5.49 – 5.35 (m, 5 H), 5.29 – 5.24 (m, 1 H), 3.91 (quint, J = 6.0 Hz, 1 H), 3.49 – 3.46 (m, 1 H), 2.78 – 2.70 (m, 2 H), 2.67 – 2.63 (m, 1 H), 2.45 – 2.43 (m, 2 H), 2.40 – 2.38 (m, 2 H), 2.35 – 2.20 (m, 5 H), 2.04 (quint, J = 7.3 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.33, 176.70, 161.44, 138.81, 135.16, 132.74,

132.27, 130.69, 130.12, 127.00, 126.96, 125.32, 71.63, 43.36, 36.96, 35.40, 33.54, 30.59, 25.99, 25.90, 22.75, 20.74, 18.23, 14.40, -4.39, -4.41 ppm; HR-MS (ESI) calcd for C₂₈H₄₄O₄SiNa [M+Na]⁺: 495.2901, found: 495.2882.

(4Z)-6-{(1*S*,5*E*)-5-[(3*S*,5*Z*,8*Z*)-3-Hydroxyundeca-5,8-dien-1-ylidene]-4-oxocyclopent-2-en-1yl}hex-4-enoic acid (28): To a stirred solution of TBS ether 124 (15 mg, 0.032 mmol, 1.0 equiv)



in MeCN (0.6 mL) at 0 °C was added dropwise a solution of HF (50 % aq., 60 μ L, ca. 1.7 mmol, ca. 50 equiv) in MeCN (0.1 mL). After stirring for 30 min, additional HF (50 % aq., 60 μ L, ca.

1.7 mmol, ca. 50 equiv) in MeCN (0.1 mL) was added. After stirring for an additional 45 min, the reaction was quenched by addition of sat. brine (3 mL) and extracted with EtOAc (3 mL). The organic extract was dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, CH₂Cl₂:EtOH, 99:1 \rightarrow 98:2 \rightarrow 97:3 \rightarrow 96:4) yielded the pure title compound (**28**, 8.9 mg, 0.026 mmol, 81 % yield) as a colorless oil.

28: $R_f = 0.60$ (CH₂Cl₂:EtOH, 9:1); $[\alpha]_D^{25} = +65.1$ (c = 0.59, CHCl₃); UV (EtOH) λ_{max} (log ε) = 245 (3.89) nm; FT-IR (neat): $v_{max} = 3408$, 3011, 2963, 2932, 1705, 1646, 1430, 1240, 1210, 1068, 1035, 839, 719 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.51 (dd, J = 5.8, 2.5 Hz, 1 H), 6.64 (t, J = 7.6 Hz, 1 H), 6.34 (dd, J = 5.9, 1.3 Hz, 1 H), 5.60 – 5.54 (m, 1 H), 5.50 – 5.34 (m, 4 H), 5.32 – 5.26 (m, 1 H), 3.88 (quint, J = 6.2 Hz, 1 H), 3.55 – 3.52 (m, 1 H), 2.82 – 2.78 (m, 2 H), 2.70 – 2.64 (m, 1 H), 2.56 – 2.45 (m, 2 H), 2.40 – 2.30 (m, 7 H), 2.06 (quint, J = 7.3 Hz, 2 H), 0.97 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.54, 176.76, 161.79, 139.56, 135.15, 132.53, 132.37, 131.95, 130.32, 126.71, 126.66, 124.73, 70.83, 43.32, 36.56, 35.00, 33.68, 30.16, 25.88, 23.03, 20.76, 14.40 ppm; HR-MS (ESI) calcd for C₂₂H₃₁O₄ [M+H]⁺: 359.2217, found: 359.2215.

Methyl (4Z)-6-{(1S,5E)-5-[(3S,5Z,8Z)-3-hydroxyundeca-5,8-dien-1-ylidene]-4-oxocyclopent-



2-en-1-yl}hex-4-enoate (29): To a stirred solution of carboxylic acid **28** (23 mg, 67 μ mol, 1.0 equiv) in C₆H₆:MeOH (3:2, 2.2 mL) at 25 °C was added dropwise a solution of trimethylsilyl

diazomethane (2 M in Et_2O , 50 μ L, 100 μ mol, 1.5 equiv) (yellow color persists). After stirring for 30 min, the reaction mixture was concentrated. Flash column chromatography

(SiO₂, hexanes:EtOAc, $3:1\rightarrow 2:1$) yielded the pure title compound (**29**, 18 mg, 48 µmol, 72 % yield) as a colorless oil.

29: $R_f = 0.57$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{25} = +147.7$ (c = 0.39, CHCl₃); UV (EtOH) λ_{max} (log ε) = 242 (4.15) nm; FT-IR (neat): $v_{max} = 3402$, 3016, 2961, 2924, 2853, 1737, 1701, 1650, 1579, 1437, 1370, 1263, 1163, 1063 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.50 (dd, J = 6.0, 2.6 Hz, 1 H), 6.54 (t, J = 6.9 Hz, 1 H), 6.34 (dd, J = 6.0, 1.8 Hz, 1 H), 5.61 – 5.53 (m, 1 H), 5.48 – 5.33 (m, 4 H), 5.31 – 5.24 (m, 1 H), 3.86 (quint, J = 6.2 Hz, 1 H), 3.66 (s, 3 H), 3.54 – 3.50 (m, 1 H), 2.80 (t, J = 7.3 Hz, 2 H), 2.71 – 2.63 (m, 1 H), 2.56 – 2.43 (m, 2 H), 2.37 – 2.24 (m, 7 H), 2.09 – 2.01 (m, 2 H), 1.97 (br s, 1 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.39, 173.61, 161.63, 139.50, 135.13, 132.48, 132.25, 131.84, 130.60, 126.72, 126.45, 124.82, 70.65, 51.78, 43.36, 36.72, 35.15, 33.92, 30.32, 25.87, 23.03, 20.74, 14.37 ppm; HR-MS (ESI) calcd for C₂₃H₃₂O₄Na [M+Na]⁺: 395.2193, found: 395.2183.

(1*E*,3*S*,9*Z*,11a*S*)-3-[(2*Z*,5*Z*)-Octa-2,5-dien-1-yl]-2,6,7,8,11,11a-hexahydro-3*H*-cyclopenta[*e*]oxacyclotridecine-5,14-dione (30): To a stirred solution of 2-methyl-6-nitrobenzoic anhydride



(53.8 mg, 156 μ mol, 1.4 equiv) and 4-dimethylaminopyridine (81.8 mg, 670 μ mol, 6.0 equiv) in CH₂Cl₂ (80 mL) was added a solution of compound **29** (40.0 mg, 112 μ mol, 1.0 equiv) in CH₂Cl₂ (40 mL) at 25 °C dropwise via syringe pump over 15 h. After stirring for an additional 2 h, the reaction

mixture was washed sequentially with sat. aq. NaHCO₃-solution (40 mL), aq. HCl (0.2 M; 40 mL), and brine (40 mL). The organic layer was dried (MgSO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes: EtOAc, 3:1) yielded pure title compound (23.7 mg, 69.6 µmol, 62 % yield) as a colorless oil.

30: $R_f = 0.54$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{24} = -9.52$ (c = 0.21, C_6H_6); IR (film): $v_{max} = 3353$, 3011, 2922, 2852, 1724, 1655, 1441, 1336, 1251, 1194, 1148, 1024, 673 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.42 (ddd, J = 6.0, 2.7, 0.9 Hz, 1 H), 6.71 (dd, J = 13.0, 4.1 Hz, 1 H), 6.45 (dd, J = 6.0, 2.0 Hz, 1 H), 5.54 – 5.47 (m, 1 H), 5.45 – 5.33 (m, 3 H), 5.34 – 5.25 (m, 1 H), 5.08 – 5.04 (m, 1 H), 5.03 – 4.95 (m, 1 H), 3.66 (br s, 1 H), 2.95 – 2.82 (m, 2 H), 2.82 – 2.74 (m, 1 H), 2.61 (dt, J = 14.5, 7.5 Hz, 1 H), 2.56 – 2.43 (m, 2 H), 2.43 – 2.27 (m, 3 H), 2.20 – 1.98 (m, 5 H), 1.01 – 0.93 (t, J = 7.6 Hz, 3 H); ¹³C-NMR (151 MHz, CDCl₃) δ 196.62, 174.46, 162.06, 139.62, 135.73, 132.61, 131.83, 129.75, 129.55, 126.68, 124.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 34.79, 31.73, 29.63, 28.21, 25.93, 124.29, 73.69, 41.53, 73.29, 73.69, 41.53, 73.29, 73.69, 41.53, 73.29, 73.69, 74.20, 73.69, 74.20, 73.69, 74.20, 73.69, 74.20, 73.69, 74.20, 73.69, 74.20, 73.69, 74.20, 74.20, 74.20, 74.20, 74.20, 74.20, 74.20, 74.20, 74.20, 74.20, 74.20, 74.20, 74.20

24.74, 20.76, 14.40 ppm; HR-MS (ESI-TOF): calcd for C₂₂H₂₈O₃Na [M+Na]⁺: 363.1931, found: 363.1939.

Synthesis of 10-Chloro- Δ^{12} -PGJ₃ Analog (**31**), its Methyl Ester (**32**) and Lactone (**33**).

(4*R*)-2-Chloro-4-{(2*Z*)-7-[(4-methoxybenzyl)oxy]hept-2-en-1-yl}cyclopent-2-en-1-one (126):



To a stirred solution of cyclopentenone **57** (332 mg, 1.00 mmol, 1.0 equiv) in methanol (10 mL) at -20 °C was added a solution of hydrogen peroxide (30 % *w/w*, 540 µL, 2.00 mmol, 2.0 equiv) in

one portion. To the above mixture was added dropwise KOH (10 % w/w, 127 µL, 0.20 mmol, 0.2 equiv) and continued to stir at -10 to -20 °C for 6 h. The reaction mixture was neutralized with 0.5 N HCl (0.3 mL), stirred for an additional 5 min at -10 °C and concentrated (removal of methanol). The resulting residual oil was taken up in EtOAc and washed with H₂O (2×10 mL), brine (5 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The crude epoxy cyclopentanone **125** was taken to the next step without further purification.

To a solution of above prepared crude epoxy cyclopentanone **125** in anhydrous acetonitrile (10 mL) at room temperature was added anhydrous LiCl (0.423 g, 10.0 mmol, 10 equiv) followed by Amberlyst-15 ion exchange resin (0.664 g, 200 wt%). The reaction flask was covered with aluminium foil and the reaction was allowed to stirr for 19 h. The reaction mixture was filtered through a plug of Celite and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 4:1 \rightarrow 2:1) yielded pure title compound (**126**, 86.0 mg, 0.240 mmol, 24 % for the two steps) as a colorless oil and alcohol **127** (57.0 mg, 0.280 mmol, 28 % for the two steps).

To a stirred solution of alcohol **127** (57.0 mg, 0.280 mmol, 1.0 equiv) and *para*-methoxy benzyloxytrichloroacetamidate in toluene (1 mL) at room temperature was added Sc(OTf)₃ (14.0 mg, 28.0 μ mol, 0.1 equiv). After stirring for 4 h at room temparature, the reaction mixture was filtered through a plug of Celite and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 4:1) yielded pure title compound (**126**, 78.0 mg, 0.220 mmol, 80 % yield) as a colorless oil.

126: $R_f = 0.60$ (hexanes: EtOAc, 4:1); $[\alpha]_D^{25} = +87.2$ (c = 1.5 in C_6H_6); IR (neat): $v_{max} = 3006$, 2981, 2936, 2861, 2845, 1722, 1612, 1596, 1512, 1456, 1247, 1033, 1016, 823 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 7.25 (d, J = 8.5 Hz, 2 H), 6.82 (d, J = 8.5 Hz, 2 H), 6.73 – 6.66 (m, 1 H), 5.32 (dt, J = 10.6, 7.4 Hz, 1 H), 4.97 – 4.88 (m, 1 H), 4.35 (s, 2 H), 3.33 – 3.31 (m, 5 H), 2.06 – 1.99

(m, 2 H), 1.80 - 1.77 (m, 2 H), 1.68 - 1.62 (m, 2 H), 1.59 - 1.50 (m, 3 H), 1.39 - 1.34 (m, 2H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 198.61, 159.77, 159.30, 136.14, 132.80, 131.37, 129.41, 125.55, 114.13, 72.88, 69.93, 54.83, 39.21, 38.10, 31.80, 29.79, 27.32, 26.65 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₅ClO₃Na [M+Na]⁺: 371.1384, found: 371.1374.

127: $R_f = 0.30$ (hexanes: EtOAc, 4:1); $[\alpha]_D^{25} = +40.0$ (c = 0.3 in C₆H₆); IR (neat): $v_{max} = 3421$, 3007, 2981, 2937, 2864, 2845, 1721, 1596, 1456, 1289, 1171, 1055, 957, 750 cm⁻¹; ¹H-NMR (600 MHz, C₆D₆) δ 6.75 (d, J = 2.5 Hz, 1 H), 5.36 – 5.28 (m, 1 H), 4.98 – 4.93 (m, 1 H), 3.41 (t, J = 6.4 Hz, 2 H), 2.11 – 2.04 (m, 2 H), 1.78 (q, J = 7.0 Hz, 2 H), 1.72 – 1.67 (m, 2 H), 1.65 – 1.58 (m, 1 H), 1.40 – 1.34 (m, 2 H), 1.31 – 1.25 (m, 2 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 199.03, 159.70, 136.03, 132.86, 125.51, 62.42, 39.23, 38.15, 32.56, 31.78, 27.27, 26.09 ppm; HR-MS (ESI-TOF): calcd for C₁₂H₁₇ClO₂ [M+Na]⁺: 229.0990, found: 229.0985.

(5Z,12E,15S,17Z)-15-{[*tert*-Butyl(dimethyl)silyl]oxy}-10-chloro-1-[(4-methoxybenzyl)oxy]prosta-5,9,12,17-tetraen-11-one (129): To a stirred solution of diisopropylamine (236 μL,



1.68 mmol, 2.1 equiv) in THF (6 mL) at 0 °C was dropwise added n-butyl lithium (1.6 M in hexanes, 1.00 mL, 1.60 mmol, 2.0 equiv). After stirring for 20 min at this temperature, the clear solution was

cooled to -78 °C and a solution of enone **126** (280 mg, 0.800 mmol, 1.0 equiv) in THF (2 mL) was added dropwise. After stirring for an additional 20 min at this temperature, a solution of aldehyde **58** (266 mg, 1.04 mmol, 1.3 equiv) in THF (8 mL) was added dropwise and stirring at this temperature was continued for an additional 30 min. The reaction mixture was then quenched with saturated aq. NH₄Cl-solution (75 mL), diluted with EtOAc (75 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with EtOAc (2 × 75 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereoisomers (**128**, 391 mg, 0.650 mmol, 81 % yield) as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of the aldol product (**128**, 391 mg, 0.650 mmol, 1.0 equiv) in CH₂Cl₂ (6 mL) at -10 °C was added DMAP (796 mg, 6.50 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (110 µL, 1.30 mmol, 2.0 equiv). After stirring for 30 min at this

temperature, the reaction mixture was allowed to warm to 25 °C and stirred for 12 h. The reaction mixture was quenched by addition of saturated aqueous NaHCO₃-solution (10 mL), diluted with CH₂Cl₂ (50 mL), the phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 50 mL), and the combined organic extracts were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 7:1) gave pure title compound (**129**, 210 mg, 0.358 mmol, 45 % yield for the two steps) as a colorless oil.

129: $R_f = 0.70$ (hexanes: EtOAc, 4:1); $[\alpha]_D^{25} = +124.2$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 3008, 2954, 2932, 2856, 1712, 1660, 1655, 1514, 1461, 1362, 1172, 1097, 1034, 835 cm⁻¹; ¹H-NMR (600 MHz, <math>C_6D_6$) δ 7.26 (d, J = 8.5 Hz, 2 H), 6.86 – 6.82 (m, 4 H), 5.53 – 5.46 (m, 1 H), 5.42 (dt, J = 9.3, 7.2 Hz, 1 H), 5.39 – 5.34 (m, 1 H), 5.10 (dt, J = 10.5, 7.3 Hz, 1 H), 4.36 (s, 2 H), 3.71 (quint, J = 5.8 Hz, 1 H), 3.35 (t, J = 6.3 Hz, 2 H), 3.32 (s, 3 H), 3.00 – 2.96 (m, 1 H), 2.39 – 2.34 (m, 1 H), 2.32 – 2.14 (m, 4 H), 1.98 – 1.87 (m, 5 H), 1.60 – 1.55 (m, 2 H), 1.43 – 1.38 (m, 2 H), 0.95 (s, 9 H), 0.90 (t, J = 7.6 Hz, 3 H), 0.06 (s, 3 H), 0.04 (s, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 187.24, 159.76, 153.40, 137.66, 137.10, 134.41, 134.22, 133.12, 131.40, 129.39, 124.98, 124.62, 114.12, 72.87, 71.70, 69.99, 54.82, 41.71, 36.87, 35.68, 30.77, 29.94, 27.51, 26.70, 26.07, 21.16, 18.27, 14.39, -4.36, -4.39 ppm; HR-MS (ESI-TOF): calcd for $C_{34}H_{51}ClO_4SiNa$ [M+Na]⁺: 609.3137, found: 609.3138.

(5Z,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-10-chloro-1-hydroxyprosta-5,9,12,17-

tetraen-11-one (130): To a vigorously stirred solution of dienone 129 (180 mg, 310 µmol,



1.0 equiv) in a mixture of CH₂Cl₂:H₂O (20:1, 5 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (139 mg, 614 μmol, 2.0 equiv). After stirring at this temperature for

2 h, the reaction mixture was diluted with Et_2O (30 mL), filtered through Celite, washed with Et_2O , and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 2:1) yielded pure title compound (**130**, 123 mg, 0.270 mmol, 86 % yield) as a colorless oil.

130: $R_f = 0.21$ (hexanes: EtOAc, 4:1); $[\alpha]_D^{25} = +56.3$ (c = 0.3 in C_6H_6); IR (film): $v_{max} = 3423$, 2932, 1709, 1654, 1559, 1538, 1460, 1256, 1062, 836 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 6.85 - 6.72 (m, 2 H), 5.51 - 5.47 (m, 1 H), 5.44 - 5.40 (m, 1 H), 5.38 - 5.33 (m, 1 H), 5.12 - 5.07 (m, 1 H),

3.72 (quint, J = 6.7 Hz, 1 H), 3.34 (t, J = 6.3 Hz, 2 H), 3.01 – 2.98 (m, 1 H), 2.39 – 2.35 (m, 1 H), 2.32 – 2.10 (m, 4 H), 1.98 – 1.91 (m, 3 H), 1.86 – 1.81 (m, 2 H), 1.27 – 1.32 (m, 2 H), 1.25 – 1.24 (m, 2 H), 0.89 (s, 9 H), 0.84 (t, J = 7.5 Hz, 3 H), 0.06 (s, 3 H), 0.04 (s, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 187.29, 153.43, 137.65, 137.10, 134.47, 134.24, 133.11, 124.95, 124.61, 71.73, 62.43, 41.72, 36.90, 35.67, 32.60, 30.77, 27.40, 26.11, 26.06, 21.15, 18.27, 14.39, –4.37, –4.39 ppm; HR-MS (ESI-TOF): calcd for C₂₆H₄₃ClO₃SiNa [M+Na]⁺: 489.2562, found: 489.2547.

(5Z,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-10-chloro-11-oxoprosta-5,9,12,17-

tetraen-1-oic acid (132): To a vigorously stirred solution of hydroxy dienone 130 (123 mg,



270 μmol, 1.0 equiv) in CH₂Cl₂ (3 mL) at 25 °C was added in one
portion pyridinium chlorochromate (104 mg, 540 μmol, 2.0 equiv).
After stirring for 2 h, the reaction mixture was diluted with Et₂O

(30 mL), filtered through Celite, washed with Et₂O, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 4:1) yielded pure title compound (**131**, 106 mg, 220 µmol, 85 % yield) as a colorless oil.

To a vigorously stirred solution of aldehyde **131** (106 mg, 220 μ mol, 1.0 equiv) in *t*-BuOH (2 mL) at 25 °C were sequentially dropwise added 2-methyl-2-butene (0.680 mL, 6.60 mmol, 30 equiv), a solution of NaH₂PO₄ (0.3 M solution in H₂O, 2.20 mL, 660 μ mol, 3.0 equiv) and a solution of NaClO₂ (80%, 73.0 mg, 0.660 μ mol, 3.0 equiv) in H₂O (1.5 mL). After stirring for 30 min, the reaction mixture was diluted with a solution of NaH₂PO₄ (4.0 g) in H₂O (80 mL) and extracted with EtOAc (5 × 40 mL). The combined organic extracts were washed with sat. brine (50 mL), dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 1:1) yielded pure title compound (**132**, 106 mg, 0.220 mmol, 99 % yield) as a colorless oil.

132: $R_f = 0.57$ (hexanes:EtOAc, 1:4); $[\alpha]_D^{25} = +59.5$ (c = 0.4 in C_6H_6); IR (film): $v_{max} = 2931$, 2857, 1710, 1660, 1559, 1460, 1406, 1255, 1087, 836 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 6.86 – 6.83 (m, 2 H), 5.52 – 5.48 (m, 1 H), 5.45 – 5.41 (m, 1 H), 5.23 – 5.19 (m, 1 H), 5.10 – 5.06 (m, 1 H), 3.73 (quint, J = 5.9 Hz, 1 H), 3.00 – 2.98 (m, 1 H), 2.37 – 2.13 (m, 5 H), 2.08 (t, J = 7.4 Hz, 2 H), 2.01 – 1.86 (m, 3 H), 1.84 – 1.74 (m, 2 H), 1.49 (quint, J = 7.4 Hz, 2 H), 0.96 (s, 9 H), 0.91 (t, J = 7.5 Hz, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 187.31, 179.62, 153.34, 137.70, 137.01, 134.58, 134.26, 131.81, 125.90, 124.60, 71.78, 41.61, 36.89, 35.66, 33.37,

30.63, 26.73, 26.07, 24.63, 21.16, 18.29, 14.40, -4.37, -4.39 ppm; HR-MS (ESI-TOF): calcd for C₂₆H₄₁ClO₄SiNa [M+Na]⁺: 503.2355, found: 503.2358.

(5Z,12E,15S,17Z)-10-Chloro-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oic acid (31): To



a stirred solution of 10-chloro- Δ^{12} -PGJ₃-15-*t*-butyldimethylsilylether (**132**, 76 mg, 0.16 mmol, 1.0 equiv) in MeCN (2.0 mL) at 0 °C was dropwise added a solution of HF (50% aq., 630 µL, ca. 16 mmol,

ca. 100 equiv) in MeCN (1.0 mL). After stirring for 45 min at this temperature, the reaction mixture was quenched with sat. brine (30 mL) and extracted with EtOAc (5×50 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 1:4) yielded pure title compound (**31**, 51 mg, 0.14 mmol, 88 % yield) as a colorless oil.

31: $R_f = 0.51$ (EtOAc); $[\alpha]_D^{25} = +95.0$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 3010, 2933, 1738, 1654, 1587, 1559, 1406, 1289, 1046, 871 cm⁻¹; ¹H-NMR (600 MHz, <math>C_6D_6$) δ 6.85 (d, J = 2.9 Hz, 1 H), 6.81 (t, J = 7.6 Hz, 1 H), 5.53 – 5.49 (m, 1 H), 5.39 – 5.35 (m, 1 H), 5.25 – 5.20 (m, 1 H), 5.11 – 5.07 (m, 1 H), 3.66 – 3.61 (m, 1 H), 2.99 – 2.96 (m, 1 H), 2.45 – 2.41 (m, 1 H), 2.33 (dt, J = 14.6, 7.2 Hz, 1 H), 2.26 – 2.19 (m, 2 H), 2.17 – 2.07 (m, 3 H), 1.98 (quint, J = 7.5 Hz, 2 H), 1.91 – 1.79 (m, 3 H), 1.50 – 1.43 (m, 2 H), 0.93 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C_6D_6) δ 187.75, 178.03, 153.76, 137.54, 135.02, 134.39, 131.94, 128.59, 125.98, 124.43, 70.91, 41.89, 36.53, 34.94, 33.06, 30.44, 26.64, 24.65, 21.10, 14.41 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₇ClO₄Na [M+Na]⁺: 389.1490, found: 389.1478.

Methyl (5Z,12E,15S,17Z)-10-chloro-15-hydroxy-11-oxoprosta-5,9,12,17-tetraen-1-oate (32): $CI \rightarrow COOMe$ $CI \rightarrow COOMe$ OH OH

32: $R_f = 0.70$ (hexanes: EtOAc, 1:1); $[\alpha]_D^{25} = +168.3$ (c = 0.1 in C_6H_6); IR (film): $v_{max} = 3441$, 2932, 1710, 1654, 1559, 1506 cm⁻¹; ¹H-NMR (600 MHz, C_6D_6) δ 6.82 – 6.79 (m, 2 H), 5.53 – 5.46 (m,

1 H), 5.32 - 5.27 (m, 1 H), 5.23 - 5.19 (m, 1 H), 5.07 - 5.02 (m, 1 H), 3.43 - 3.38 (m, 1 H), 3.34 (s, 3 H), 2.94 - 2.91 (m, 1 H), 2.34 - 2.29 (m, 1 H), 2.18 (dt, J = 14.8, 7.4 Hz, 1 H), 2.11 - 2.02 (m, 4 H), 1.97 - 1.87 (m, 3 H), 1.83 - 1.77 (m, 2 H), 1.55 - 1.46 (m, 2 H), 1.41 (d, J = 4.3 Hz, 1 H), 0.88 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 187.37, 173.39, 153.32, 137.66, 137.33, 134.98, 134.23, 132.00, 125.68, 124.56, 70.37, 51.11, 41.53, 36.64, 35.37, 33.23, 30.31, 26.82, 24.87, 21.07, 14.40 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₂₉ClO₄Na [M+Na]⁺: 403.1647, found: 403.1659.

(5Z,12E,15S,17Z)-10-Chloro-1,15-epoxyprosta-5,9,12,17-tetraene-1,11-dione (33): To a



stirred solution of 2-methyl-6-nitrobenzoic anhydride (28.0 mg, 82.0 μ mol, 1.5 equiv) and 4-dimethylaminopyridine (26.7 mg, 218 μ mol, 4.0 equiv) in CH₂Cl₂ (40 mL) was added a solution of carboxylic acid **31** (20.0 mg,

54.6 µmol, 1.0 equiv) in CH₂Cl₂ (20 mL) at 25 °C dropwise via syringe pump over 10 h. After stirring for an additional 2 h, the reaction mixture was washed sequentially with sat. aq. NaHCO₃-solution (10 mL), aq. HCl (0.2 M, 10 mL), and sat. brine (10 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated. Flash column chromatography (SiO₂, hexanes:EtOAc, 3:1) yielded pure title compound (**33**, 14.8 mg, 40.0 µmol, 73 % yield) as a light yellow solis. **33**: $R_f = 0.35$ (hexanes:EtOAc, 3:1); mp = 102–106 °C; $[\alpha]_D^{25} = +3.5$ (*c* = 0.7 in C₆H₆); IR (film): $v_{max} = 3011$, 2963, 2931, 1718, 1702, 1662, 1587, 1279, 1164, 1033, 941, 893 cm⁻¹; ¹H-NMR (600 MHz, C₆D₆) δ 6.59 – 6.56 (m, 2 H), 5.49 – 5.44 (m, 1 H), 5.27 – 5.22 (m, 1 H), 5.10 – 5.03 (m, 2 H), 4.96 – 4.92 (m, 1 H), 2.09 – 2.97 (m, 1 H), 2.40 (ddd, *J*=14.6, 9.8, 5.2 Hz, 1 H), 2.29 – 2.21 (m, 3 H), 2.19 – 2.14 (m, 1 H), 2.04 (ddd, *J*=15.4, 8.9, 3.2 Hz, 1 H), 1.98 – 1.86 (m, 5 H), 1.75 – 1.69 (m, 1 H), 1.28 – 1.19 (m, 2 H), 0.89 (t, *J*=7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 187.12, 172.16, 152.78, 138.06, 137.61, 135.16, 133.43, 132.30, 124.71, 123.28, 72.60, 41.28, 33.52, 32.76, 32.04, 28.43, 25.99, 24.56, 21.04, 14.35 ppm; HR-MS (ESI-TOF): calcd for

C₂₀H₂₅ClO₃Na [M+Na]⁺: 371.1384, found: 371.1395.

<u>Synthesis of 8-Methyl- Δ^{12} -PGJ₃ Analogs 34–37.</u>

5-Methyl-3-{[(1*R*,2*S*,5*R*)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}cyclopent-2-en-1-one (134):

To a stirred solution of diisopropylamine (2.83 g, 3.91 mL, 27.9 mmol, 1.10 equiv) in THF (30 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M 134 in hexane, 10.7 mL, 26.7 mmol, 1.05 equiv). The resulting solution was stirred Me '''Me at 0 °C for 1 h and then cooled to -78 °C. A solution of ketone **133** (6.00 g, Mé 25.4 mmol, 1.00 equiv) in THF (10 mL) was added dropwise over a period of 30 min. The resulting yellow solution was stirred at -78 °C for 45 min and methyl iodide (4.68 g, 2.06 mL, 33.0 mmol, 1.30 equiv) was added dropwise over a period of 30 min. After 5 min, 1,3-dimethyl-2imidazolidinone (3.48 g, 3.29 mL, 30.5 mmol, 1.20 equiv) was added dropwise. After stirring at the same temperature for an additional 12 h, the reaction mixture was warmed to 25 °C and partitioned between saturated aq. NH₄Cl-solution (20 mL) and EtOAc (80 mL). The organic layer was separated and washed sequentially with H_2O (20 mL) and brine (20 mL), and the combined aqueous layers were back-extracted with EtOAc (3×30 mL). The combined organic extracts were dried (MgSO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:Et₂O, 3:1) gave title compound (134, 4.85 g, 19.4 mmol, 76 % yield, mixture of diastereomers) as a colorless oil.

134: $R_f = 0.39$ (hexanes:Et₂O, 1:1); IR (film): $v_{max} = 2955$, 2927, 2870, 1695, 1586, 1455, 1332, 1249, 1194, 982, 966, 819 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃, mixture of diastereomers) δ 5.23 (s, 1 H), 3.94 (tt, J = 10.7, 3.9 Hz, 1 H), 2.80 (dddd, J = 27.1, 17.5, 7.3, 1.1 Hz, 1 H), 2.54 – 2.44 (m, 1 H), 2.18 (dddd, J = 28.9, 17.6, 2.9, 1.1 Hz, 1 H), 2.11 (dtt, J = 11.9, 3.7, 1.8 Hz, 1 H), 1.98 (dddd, J = 14.0, 9.4, 5.7, 2.3 Hz, 1 H), 1.75 – 1.67 (m, 3 H), 1.52 – 1.47 (m, 1 H), 1.45 – 1.41 (m, 1 H), 1.20 (d, J = 7.4, 3 H), 1.10 – 0.99 (m, 2 H), 0.95 – 0.88 (m, 6 H), 0.76 – 0.74 (m, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃, mixture of diastereomers) δ 209.12, 188.05, 188.04, 102.99, 102.93, 82.40, 82.39, 47.54, 47.52, 39.61, 39.56, 39.52, 39.48, 37.64, 37.63, 34.25, 31.49, 26.46, 26.40, 23.73, 23.67, 22.09, 20.70, 20.68, 16.92, 16.91, 16.79, 16.75 ppm; HR-MS (ESI-TOF): calcd for C₁₆H₂₇O₂ [M+H]⁺: 251.2006, found: 251.1996.

5-{(2Z)-7-[(4-Methoxybenzyl)oxy]hept-2-en-1-yl}-5-methyl-3-{[(1R,2S,5R)-5-methyl-2-(propan-2-yl)cyclohexyl]oxy}cyclopent-2-en-1-one (136): To a stirred solution



diisopropylamine (2.98 mL, 21.3 mmol, 1.10 equiv) in THF (30 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M in hexane, 8.12 mL, 20.3 mmol, 1.05 equiv). The resulting solution was stirred at 0 °C for 1 h and then cooled to -78 °C. A solution of ketone **134** (4.84 g, 19.3 mmol,

of

1.00 equiv) in THF (30 mL) was added dropwise over a period of 30 min. The resulting yellow solution was stirred at -78 °C for 45 min and allylic bromide **135** (7.87 g, 25.1 mmol, 1.30 equiv) in THF (5 mL) was added dropwise over a period of 30 min. After 5 min, 1,3-dimethyl-2-imidazolidinone (2.65 g, 2.50 mL, 23.2 mmol, 1.20 equiv) was added dropwise. After stirring at the same temperature for an additional 2 h, the reaction mixture was slowly warmed to -40 °C and stirred for an additional 8 h. The reaction mixture was warmed to 25 °C and partitioned between saturated aqueous NH₄Cl-solution (20 mL) and EtOAc (60 mL). The organic layer was separated and washed sequentially with H₂O (20 mL) and saturated aqueous NaCl-solution (20 mL), and the combined aqueous layers were back-extracted with EtOAc (3 × 25 mL). The combined organic extracts were dried (MgSO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexane:EtOAc, 4:1) gave title compound (**136**, 6.85 g, 14.2 mmol, 73 % yield, mixture of diastereomers) as a colorless oil.

136: $R_f = 0.64$ (hexanes:EtOAc, 2:1); IR (film): $v_{max} = 2953$, 2927, 2868, 1691, 1579, 1512, 1331, 1245, 1096, 1035, 823 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃, mixture of diastereomers) δ 7.25 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.3 Hz, 2 H), 5.50 – 5.41 (m, 1 H), 5.27 – 5.17 (m, 2 H), 4.42 (s, 2 H), 3.97 – 3.89 (m, 1 H), 3.80 (s, 3 H), 3.43 (td, J = 6.6, 1.7 Hz, 2 H), 2.54 – 2.45 (m, 1 H), 2.30 – 2.16 (m, 3 H), 2.13 – 2.01 (m, 3 H), 2.01 – 1.90 (m, 1 H), 1.74 – 1.66 (m, 3 H), 1.63 – 1.56 (m, 2 H), 1.53 – 1.44 (m, 1 H), 1.46 – 1.37 (m, 3 H), 1.15 – 1.14 (m, 3 H), 1.10 – 0.99 (m, 2 H), 0.96 – 0.88 (m, 6 H), 0.76 – 0.74 (m, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃, mixture of diastereomers) δ 210.52, 210.47, 187.38, 187.28, 159.23, 132.83, 132.78, 130.89, 129.34, 124.84, 124.77, 113.89, 102.43, 102.31, 82.48, 82.36, 72.66, 70.11, 55.41, 47.56, 47.50, 47.04, 46.98, 41.80, 41.78, 39.69, 39.53, 35.66, 35.29, 34.26, 31.50, 31.49, 29.55, 29.53, 27.26, 27.24, 26.61, 26.50, 26.43, 26.38, 24.07, 23.86, 23.81, 23.76, 22.10, 22.09, 20.66, 20.58, 16.88, 16.79 ppm; HR-MS (ESI-TOF): calcd for C₃₁H₄₆O₄Na[M+Na]⁺: 505.3288, found: 505.3270.

4-{(2Z)-7-[(4-Methoxybenzyl)oxy]hept-2-en-1-yl}-4-methylcyclopent-2-en-1-one (137): To a



solution was cooled to -78 °C and quenched with MeOH (2 mL), diluted with Et₂O (50 mL) and allowed to warm to 25 °C. Under vigorous stirring, saturated Na-K tartrate-solution (50 mL) was added and the resulting mixture was stirred for an additional 3 h. The resultant biphasic mixture was extracted with EtOAc (3 × 100 mL), and the combined organic extracts were washed sequentially with H₂O (40 mL) and brine (40 mL), dried (MgSO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 10:1 \rightarrow 3:1) gave pure title compound (**137**, 3.54 g, 10.8 mmol, 76% yield, mixture of enantiomers) as a colorless oil.

137: $R_f = 0.53$ (hexanes: EtOAc, 2:1); IR (film): $v_{max} = 3007$, 2932, 2858, 1711, 1611, 1511, 1456, 1301, 1245, 1172, 1095, 1033, 817 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.42 (d, J = 5.6 Hz, 1 H), 7.25 (d, J = 8.8 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.04 (d, J = 5.6 Hz, 1 H), 5.56 – 5.45 (m, 1 H), 5.32 – 5.23 (m, 1 H), 4.42 (s, 2 H), 3.80 (s, 3 H), 3.43 (t, J = 6.5 Hz, 2 H), 2.29 (d, J = 18.5 Hz, 1 H), 2.27 (ddd, J = 14.4, 8.3, 1.4 Hz, 1 H), 2.16 (ddd, J = 14.2, 6.9, 1.5 Hz, 1 H), 2.10 (d, J = 18.5 Hz, 1 H), 2.05 – 1.99 (m, 2 H), 1.63 – 1.56 (m, 2 H), 1.42 (dq, J = 9.7, 7.5 Hz, 2 H), 1.22 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 209.89, 172.61, 159.25, 133.29, 132.21, 130.83, 129.34, 124.42, 113.89, 72.69, 70.02, 55.40, 47.64, 45.27, 37.89, 29.52, 27.25, 26.30, 26.22 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₂₈O₃Na [M+Na]⁺: 351.1931, found: 351.1914.

(5Z,12E,15S,17Z)-15-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-[(4-methoxybenzyl)oxy]-8-methylprosta-5,9,12,17-tetraen-11-one (139): To a stirred solution of diisopropylamine (1.58 g,



2.19 mL, 15.6 mmol, 2.05 equiv) in THF (100 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M in hexanes, 6.09 mL, 15.2 mmol, 2.00 equiv). After stirring for 20 min at this temperature,

the clear solution was cooled to -78 °C and a solution of enone **137** (2.50 g, 7.61 mmol, 1.0 equiv) in THF (60 mL) was added dropwise. After stirring for an additional 20 min at this temperature, a solution of aldehyde **58** (2.34 g, 9.13 mmol, 1.2 equiv) in THF (60 mL) was added dropwise and stirring at this temperature was continued for an additional 75 min. The reaction mixture was then
quenched with saturated aqueous NH₄Cl-solution (120 mL), diluted with EtOAc (150 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with EtOAc (3×100 mL), and the combined organic extracts were washed with brine (100 mL), dried (MgSO₄), filtered, and concentrated under reduced pressure. The crude aldol product was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereoisomers (763 mg, 1.30 mmol, 17 % yield) as a colorless oil, which was taken to the next step without further purification and to recover unreacted starting material **137** (1.75 g, 5.33 mmol).

To a stirred solution of the aldol product (763 mg, 1.30 mmol, 1.00 equiv) in CH₂Cl₂ (15 mL) at -10 °C was added DMAP (1.59 g, 13.0 mmol, 10.0 equiv), and then, slowly and dropwise, methanesulfonyl chloride (299 mg, 202 µL, 2.61 mmol, 2.00 equiv). After stirring for 30 min at this temperature, the reaction mixture was brought to 25 °C and stirred for 10 h. The reaction mixture was quenched with saturated aqueous NaHCO₃-solution (20 mL), diluted with CH₂Cl₂ (100 mL), the phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 100 mL), and the combined organic extracts were washed with H₂O (50 mL), dried (MgSO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 8:1) gave pure title compound (**139**, 499 mg, 880 µmol, 67 % yield, mixture of diastereomers, 1:2 dr) as a colorless oil.

139: $R_f = 0.71$ (hexanes:EtOAc, 2:1); IR (film): $v_{max} = 3009$, 2955, 2930, 2856, 1703, 1651, 1612, 1586, 1512, 1462, 1360, 1247, 1084, 833, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃, mixture of diastereomers) δ 7.28 – 7.19 (m, 3 H), 6.90 – 6.84 (m, 2 H), 6.64 – 6.56 (m, 1 H), 6.22 (d, *J*=5.9 Hz, 1 H), 5.51 – 5.43 (m, 1 H), 5.44 – 5.31 (m, 2 H), 5.20 – 5.09 (m, 1 H), 4.42 (s, 2 H), 3.88 – 3.81 (m, 1 H), 3.79 (s, 3 H), 3.42 (t, *J*=6.5 Hz, 2 H), 2.54 – 2.35 (m, 4 H), 2.30 – 2.19 (m, 2 H), 2.07 – 1.94 (m, 4 H), 1.62 – 1.54 (m, 2 H), 1.44 – 1.35 (m, 2 H), 1.34 – 1.32 (m, 3 H), 0.96 – 0.94 (m, 3 H), 0.89 – 0.87 (m, 9 H), 0.09 – 0.03 (m, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃, mixture of diastereomers) δ 196.73, 196.72, 167.53, 167.49, 159.23, 142.13, 142.08, 134.11, 132.67, 132.60, 132.56, 132.49, 132.42, 130.81, 129.30, 124.52, 124.50, 124.43, 124.40, 113.87, 72.67, 71.97, 71.87, 70.04, 55.37, 47.70, 36.06, 36.02, 35.69, 35.55, 29.54, 27.36, 27.33, 26.31, 26.29, 25.98, 25.97, 24.20, 24.03, 20.90, 18.18, 18.17, 14.31, -4.38, -4.39, -4.43 ppm; HR-MS (ESI-TOF): calcd for C₃₅H₅₄O₄SiNa [M+Na]⁺: 589.3684, found: 589.3672.

(5Z,12E,15S,17Z)-15-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-hydroxy-8-methylprosta-5,9,12,17tetraen-11-one (140): To a vigorously stirred solution of compound 139 (378 mg, 667 μmol,



1.0 equiv) in a mixture of CH₂Cl₂:H₂O (20:1; 4 mL) at 0 °C was added in one portion 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (303 mg, 1.33 mmol, 2.0 equiv). After stirring at this temperature for 45 min, the reaction mixture was diluted with Et₂O (30 mL), filtered through

Celite, washed with Et_2O , and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 2:1) yielded pure title compound (**140**, 261 mg, 584 µmol, 88 % yield, mixture of diastereomers, 1:2 dr) as a colorless oil.

140: $R_f = 0.29$ (hexanes: EtOAc, 2:1); IR (film): $v_{max} = 3406$, 3011, 2956, 2929, 2857, 1698, 1648, 1586, 1461, 1254, 1067, 835, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃, mixture of diastereomers) δ 7.26 – 7.21 (m, 1 H), 6.63 – 6.56 (m, 1 H), 6.23 (d, J = 5.9 Hz, 1 H), 5.51 – 5.31 (m, 3 H), 5.22 – 5.11 (m, 1 H), 3.85 (p, J = 6.0 Hz, 1 H), 3.63 (t, J = 6.5 Hz, 2 H), 2.55 – 2.35 (m, 4 H), 2.32 – 2.19 (m, 2 H), 2.07 – 1.97 (m, 4 H), 1.59 – 1.51 (m, 2 H), 1.43 – 1.37 (m, 2 H), 1.35 – 1.33 (m, 3 H), 0.97 – 0.94 (m, 3 H), 0.88 – 0.87(m, 9 H), 0.08 – 0.02 (m, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃, mixture of diastereomers) δ 196.79, 196.77, 167.53, 167.49, 142.16, 142.12, 134.16, 132.74, 132.65, 132.52, 132.47, 132.41, 124.60, 124.57, 124.53, 72.02, 71.90, 62.90, 62.89, 47.73, 36.10, 36.07, 35.69, 35.58, 32.49, 32.47, 27.30, 27.26, 26.00, 25.99, 25.84, 24.21, 24.04, 20.93, 18.21, 18.20, 14.33, -4.36, -4.37, -4.41 ppm; HR-MS (ESI-TOF): calcd for C₂₇H₄₆O₃SiNa [M+Na]⁺: 469.3108, found: 469.3094.

(5Z,12E,15S,17Z)-15-{[tert-Butyl(dimethyl)silyl]oxy}-8-methyl-11-oxoprosta-5,9,12,17-

tetraen-1-oic acid (141): To a vigorously stirred solution of primary alcohol 140 (248 mg,



554 μ mol, 1.0 equiv) in CH₂Cl₂ (5 mL) at 25 °C was added in one portion pyridiniumchlorochromate (358 mg, 1.66 mmol, 2.0 equiv). After stirring for 2 h, the reaction mixture was diluted with Et₂O

(30 mL), filtered through Celite, washed with Et₂O, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 6:1) yielded the corresponding aldehyde (203 mg, 456 µmol) as a colorless oil that was immediately used in the next step.

To a vigorously stirred solution of the obtained aldehyde (203 mg, 456 μ mol, 1.0 equiv) in *t*-BuOH (6 mL) at 25 °C were sequentially dropwise added 2-methyl-2-butene (320 mg, 484 μ L,

4.56 mmol, 10.0 equiv), a solution of NaH₂PO₄ (164 mg, 1.37 mmol, 3 equiv) in H₂O (2.25 mL) and a solution of NaClO₂ (80%; 154 mg, 1.37 mmol, 3.0 equiv) in H₂O (2.25 mL). After stirring for 30 min, the reaction mixture was diluted with a solution of NaH₂PO₄ (4.0 g) in H₂O (80 mL) and extracted with EtOAc (5×80 mL). The combined organic extracts were washed with brine (50 mL), dried (MgSO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 1:1) yielded pure title compound (**141**, 199 mg, 432 µmol, 78% for the two steps, mixture of diastereomers, 2:1 dr) as a colorless oil.

141: $R_f = 0.20$ (hexanes:EtOAc, 1:1); IR (film): $v_{max} = 3403$, 2959, 2928, 1707, 1645, 1456, 1248, 1183, 1055, 974, 836 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃, mixture of diastereomers) δ 7.26 – 7.18 (m, 1 H), 6.66 – 6.56 (m, 1 H), 6.25 (d, J = 5.9 Hz, 1 H), 5.52 – 5.32 (m, 3 H), 5.32 – 5.16 (m, 1 H), 3.90 – 3.80 (m, 1 H), 2.55 – 2.37 (m, 4 H), 2.34 (t, J = 7.4 Hz, 2 H), 2.31 – 2.16 (m, 2 H), 2.12 – 1.97 (m, 4 H), 1.73 – 1.63 (m, 2 H), 1.36 – 1.33 (m, 3 H), 0.95 (t, J = 7.5 Hz, 3 H), 0.90 – 0.87 (m, 9 H), 0.09 – 0.03 (m, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃, mixture of diastereomers) δ 196.79, 196.76, 177.97, 167.46, 167.41, 142.11, 142.08, 134.22, 132.79, 132.74, 132.65, 131.33, 131.29, 125.58, 124.52, 72.14, 71.99, 48.01, 47.68, 36.10, 36.06, 36.04, 36.00, 35.65, 35.57, 33.25, 33.21, 26.79, 26.74, 26.01, 26.00, 24.58, 24.55, 24.19, 24.03, 20.94, 20.87, 18.24, 18.23, 14.33, -4.35, -4.36, -4.39 ppm; HR-MS (ESI-TOF): calcd for C₂₇H₄₄O₄SiNa [M+Na]⁺: 483.2901, found: 483.2901.

(5Z,12E,15S,17Z)-15-Hydroxy-8-methyl-11-oxoprosta-5,9,12,17-tetraen-1-oic acid (142): To



a stirred solution of compound **141** (140 mg, 304 μ mol, 1.0 equiv) in MeCN (3.0 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 530 μ L, ca. 15.2 mmol, ca. 50 equiv) in MeCN (3.0 mL). After

stirring for 75 min at this temperature, the reaction mixture was quenched by addition of sat. brine (30 mL) and extracted with EtOAc (5 × 50 mL). The combined organic extracts were dried (MgSO₄), filtered, and concentrated under reduced pressure to a volume of ca. 1 mL (not to dryness!). Flash column chromatography (SiO₂, hexanes:EtOAc, 10:1 \rightarrow 1:1) yielded pure title compound (**142**, 79.0 mg, 228 µmol, 75 % yield, mixture of diastereomers, 2:1 dr) as a colorless oil.

142: $R_f = 0.40$ (hexanes: EtOAc, 1:4); IR (film): $v_{max} = 3412$, 2960, 2931, 1716, 1653, 1459, 1376, 1244, 1062 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃, mixture of diastereomers) δ 7.31 (t, J = 6.2 Hz,

1 H), 6.64 – 6.54 (m, 1 H), 6.27 (d, J=5.9 Hz, 1 H), 5.64 – 5.56 (m, 1 H), 5.47 – 5.41 (m, 1 H), 5.41 – 5.34 (m, 1 H), 5.28 – 5.19 (m, 1 H), 3.89 – 3.81 (m, 1 H), 2.63 – 2.47 (m, 3 H), 2.37 – 2.28 (m, 4 H), 2.15 – 2.01 (m, 5 H), 1.73 – 1.63 (m, 2 H), 1.37 – 1.35 (m, 3 H), 0.97 (t, J=7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃, mixture of diastereomers) δ 196.91, 196.90, 177.75, 167.72, 167.69, 143.12, 143.10, 135.93, 135.92, 132.67, 131.64, 131.45, 125.44, 125.34, 123.86, 123.83, 71.23, 70.95, 47.72, 47.66, 35.98, 35.95, 35.74, 35.64, 34.87, 34.84, 33.27, 33.17, 26.77, 26.68, 24.67, 24.55, 24.01, 23.86, 20.92, 20.88, 14.38, 14.35 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₃₀O₄Na [M+Na]⁺: 369.2036, found: 369.2021.

Methyl (5Z,12E,15S,17Z)-15-hydroxy-8-methyl-11-oxoprosta-5,9,12,17-tetraen-1-oate (34) and methyl $(5Z,8\beta,12E,15S,17Z)$ -15-hydroxy-8-methyl-11-oxoprosta-5,9,12,17-tetraen-1oate (36): To a stirred solution of compound 142 (20.0 mg, 60.2 µmol, 1.0 equiv) in C₆H₆:MeOH



(3:2, 1.5 mL) at 25 °C was dropwise added a solution of trimethylsilyl diazomethane (2.0 M in Et₂O, 60.0 μ L, 120 μ mol, 1.5 equiv) (yellow color persists). After stirring for 30 min, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 2:1) gave pure title compounds (**34**, 12.4 mg, 34.4 μ mol, 57 % yield, and **36**, 5.52 mg,

16.1 µmol, 27 % yield) as colorless oils.

34: $R_f = 0.56$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{24} = +46.1$ (c = 0.18, C_6H_6); IR (film): $v_{max} = 3461$, 3011, 2958, 2928, 2872, 1736, 1702, 1649, 1454, 1436, 1210, 1170, 1053, 815 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.26 (dd, J = 5.9, 0.9 Hz, 1 H), 6.61 (t, J = 7.7 Hz, 1 H), 6.26 (d, J = 5.9 Hz, 1 H), 5.64 – 5.56 (m, 1 H), 5.43 – 5.34 (m, 2 H), 5.19 (dtt, J = 10.8, 7.5, 1.6 Hz, 1 H), 3.82 (pd, J = 6.2, 3.7 Hz, 1 H), 3.67 (s, 3 H), 2.52 (ddd, J = 7.6, 6.3, 4.0 Hz, 2 H), 2.48 (ddd, J = 7.4, 3.1, 1.5 Hz, 2 H), 2.33 – 2.27 (m, 4 H), 2.12 – 2.03 (m, 2 H), 2.06 – 2.00 (m, 2 H), 1.93 (d, J = 3.9 Hz, 1 H), 1.66 (p, J = 7.4 Hz, 2 H), 1.37 (s, 3 H), 0.97 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.69, 174.03, 167.50, 142.62, 135.68, 132.59, 131.48, 131.38, 125.14, 123.83, 70.79, 51.56, 47.59, 35.83, 35.70, 34.99, 33.36, 26.74, 24.62, 24.10, 20.78, 14.21 ppm; HR-MS (ESI-TOF): calcd for C₂₂H₃₂O₄Na [M+Na]⁺: 383.2193, found: 383.2174.

36: $R_f = 0.50$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{24} = -17.6$ (c = 0.33, C_6H_6); IR (film): $v_{max} = 3423$, 2956, 2923, 2852, 1736, 1649, 1454, 1439, 1259, 1169, 808 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.19

(dd, J = 6.0, 0.8 Hz, 1 H), 6.55 (t, J = 7.7 Hz, 1 H), 6.19 (d, J = 5.9 Hz, 1 H), 5.57 – 5.50 (m, 1 H), 5.37 – 5.27 (m, 2 H), 5.15 – 5.08 (m, 1 H), 3.80 – 3.72 (m, 1 H), 3.60 (s, 3 H), 2.49 (ddd, J = 15.3, 8.1, 7.2 Hz, 1 H), 2.45 – 2.35 (m, 3 H), 2.23 (t, J = 7.3 Hz, 4 H), 2.04 – 1.91 (m, 4 H), 1.74 (d, J = 3.8 Hz, 1 H), 1.59 (p, J = 7.2 Hz, 2 H), 1.32 (s, 3 H), 0.91 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.83, 174.08, 167.66, 142.90, 135.92, 132.72, 131.61, 131.42, 125.27, 123.93, 70.83, 51.70, 47.77, 35.99, 35.77, 35.14, 33.51, 26.90, 24.78, 24.33, 20.94, 14.36 ppm; HR-MS (ESI-TOF): calcd for C₂₂H₃₂O₄Na [M+Na]⁺: 383.2193, found: 383.2179.

(5*Z*,12*E*,17*Z*)-8-Methyl-1,15-epoxyprosta-5,9,12,17-tetraene-1,11-dione (35) and (5*Z*,8β,12*E*,17*Z*)-8-Methyl-1,15-epoxyprosta-5,9,12,17-tetraene-1,11-dione (37): To a stirred



solution of 2-methyl-6-nitrobenzoic anhydride (69.6 mg, 202 μ mol, 1.4 equiv) and 4-dimethylaminopyridine (106 mg, 866 μ mol, 6.0 equiv) in CH₂Cl₂ (100 mL) was added a solution of compound **142** (50.0 mg, 144 μ mol, 1.0 equiv) in CH₂Cl₂ (50 mL) at 25 °C dropwise via syringe pump over 15 h. After stirring for an additional 2 h, the reaction mixture was washed sequentially with sat. aq. NaHCO₃-solution (50 mL), aq. HCl (0.2 M; 50 mL), and brine (50 mL). The organic layer was dried (MgSO₄), filtered,

and concentrated. Flash column chromatography (SiO₂, hexanes: EtOAc, 3:1) yielded pure title compounds (**35**, 17.9 mg, 54.5 μ mol, 38 % yield, and **37**, 10.1 mg, 30.8 μ mol, 21 % yield) as colorless oils.

35: $R_f = 0.48$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{24} = +43.0$ (c = 0.384, C_6H_6); IR (film): $v_{max} = 3010$, 2962, 2930, 2872, 1729, 1705, 1654, 1585, 1455, 1239, 1155, 1045, 829 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.23 (dd, J = 5.9, 0.9 Hz, 1 H), 6.39 (ddd, J = 12.3, 3.1, 0.9 Hz, 1 H), 6.28 (d, J = 5.9 Hz, 1 H), 5.62 – 5.54 (m, 1 H), 5.36 (dtt, J = 10.8, 7.5, 1.6 Hz, 1 H), 5.28 – 5.21 (m, 1 H), 5.13 – 5.02 (m, 2 H), 3.07 (dd, J = 14.5, 11.3 Hz, 1 H), 2.86 (ddd, J = 15.6, 12.3, 11.1 Hz, 1 H), 2.69 (ddt, J = 14.1, 11.5, 8.4 Hz, 1 H), 2.55 – 2.49 (m, 1 H), 2.48 – 2.43 (m, 1 H), 2.41 (ddd, J = 15.7, 3.2, 2.3 Hz, 1 H), 2.32 (ddd, J = 15.3, 10.4, 2.4 Hz, 1 H), 2.19 (ddd, J = 15.3, 8.4, 2.3 Hz, 1 H), 2.14 – 2.06 (m, 3 H), 1.88 – 1.78 (m, 1 H), 1.73 (dddd, J = 19.0, 10.7, 4.4, 2.3 Hz, 1 H), 1.40 (s, 3 H), 1.40 – 1.30 (m, 1 H), 0.99 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.55, 173.03, 166.92, 142.80, 135.47, 133.07, 131.73, 131.46, 125.44, 122.82, 73.41, 48.03, 35.78, 34.06, 32.98, 125.24 (m, 1 H), 1.20 (m, 1 H), 1.40 (m, 1 H), 1.20 (m

32.60, 26.06, 25.97, 24.79, 20.90, 14.31 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₂₈O₃Na [M+Na]⁺: 351.1931, found: 351.1921.

37: $R_f = 0.53$ (hexanes:EtOAc, 2:1); $[\alpha]_D^{24} = +4.93$ (c = 0.142, C_6H_6); IR (film): $v_{max} = 3010$, 2963, 2931, 2871, 1763, 1730, 1703, 1652, 1538, 1455, 1346, 1241, 1211, 1165, 1062, 804 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.21 (dd, J = 6.0, 0.9 Hz, 1 H), 6.71 (dd, J = 12.2, 2.7 Hz, 1 H), 6.34 (d, J = 5.9 Hz, 1 H), 5.56 – 5.47 (m, 1 H), 5.32 – 5.24 (m, 1 H), 5.23 – 5.16 (m, 1 H), 5.13 (dtd, J = 9.3, 5.0, 1.8 Hz, 1 H), 5.00 (tt, J = 10.6, 2.6 Hz, 1 H), 3.02 (ddd, J = 16.8, 12.3, 4.8 Hz, 1 H), 2.90 (dd, J = 15.9, 10.3 Hz, 1 H), 2.63 – 2.56 (m, 1 H), 2.53 – 2.45 (m, 1 H), 2.35 – 2.27 (m, 3 H), 2.23 – 2.16 (m, 1 H), 2.13 – 2.05 (m, 3 H), 1.91 – 1.81 (m, 2 H), 1.50 – 1.42 (m, 1 H), 1.35 (s, 3 H), 0.97 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.87, 173.03, 167.65, 142.77, 135.30, 133.15, 130.76, 128.85, 125.53, 123.39, 71.51, 47.70, 35.06, 32.25, 30.92, 29.27, 25.54, 25.04, 23.49, 20.96, 14.30 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₂₈O₃Na [M+Na]⁺: 351.1931, found: 351.1919.

Synthesis of 15-Fluoro- Δ^{12} -PGJ₃ Analog **29**, and its Methyl Ester **30**

$(5Z, 12E, 15R, 17Z) - 15 - \{[tert-Butyl(dimethyl)silyl] oxy\} - 1 - [(4-methoxybenzyl) oxy] prosta-5, 9, 12, 17 - 100 -$

tetraen-11-one (144): To a stirred solution of diisopropyl amine (270 µL, 1.93 mmol, 2.2 equiv) in



THF (8 mL) at 0 °C was added *n*-butyl lithium (1.6 M in hexanes, 1.10 mL, 1.76 mmol, 2.0 equiv) dropwise. After stirring at 0 °C for 20 min the resulting solution was cooled to -78 °C and a solution of

enone **57** (275 mg, 0.875 mmol, 1.0 equiv) in THF (6 mL) was added dropwise. After stirring at $-78 \degree$ C for 30 min, a solution of aldehyde *ent*-**58** (270 mg, 1.06 mmol, 1.2 equiv) in THF (6 mL) was added dropwise. After stirring at the same temperature for additional 30 min the reaction mixture was quenched by addition of sat. aq. NH₄Cl-solution (30 mL) and warmed to 25 °C. The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine (30 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The residue was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereomers (ca. 6:1, judged by ¹H-HMR, 430 mg, 0.750 mmol, 86 % yield) as a light yellow oil, which was used in the next step without further purification.

The crude aldol product **143** (418 mg, 0.732 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (9 mL) and cooled to 0 °C. Triethylamine (1.02 mL, 7.32 mmol, 10 equiv) was added to the above

solution followed by dropwise addition of methanesulfonyl chloride (283 μ L, 3.66 mmol, 5.0 equiv). After stirring at the same temperature for 5 min, the reaction mixture was quenched with saturated aq. NaHCO₃-solution (40 mL), diluted with CH₂Cl₂ (40 mL) and warmed to 25 °C. The aqueous layer was extracted with CH₂Cl₂ (2 × 50 mL). The combined organic extracts were washed with water (20 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was filtered through a short column (SiO₂, hexanes:EtOAc, 2:1) to obtained the crude mesylate (438 mg, 0.674 mmol, 92 % yield) as a yellow oil, which was used in the next step without further purification.

The above crude mesylate (438 mg, 0.674 mmol, 1.0 equiv) was dissolved in CH₂Cl₂ (15 mL) and neutral alumina (481 mg, 4.72 mmol, 7.0 equiv) was added at 25 °C. The reaction mixture was stirred at 25 °C for 8 h, during which time neutral alumina (5×481 mg, 5×4.72 mmol, 5×7.0 equiv) was added every 1.5 h. Upon completion of the reaction as indicated by thin-layer chromatography (TLC), the reaction mixture was filtered through a pad of Celite, rinsed with EtOAc and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 10:1) gave pure title compound (**144**, 264 mg, 0.477 mmol, 65 % yield from **143**) as a yellow oil.

144: $R_f = 0.58$ (hexanes:EtOAc, 3:1); $[\alpha]_D^{25} = +87.2$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 2930$, 2856, 1704, 1656, 1513, 1247, 1095, 835, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.46 (ddd, J = 6.1, 2.7, 1.0 Hz, 1 H), 7.25 (d, J = 8.5 Hz, 2 H), 6.87 (d, J = 8.5 Hz, 2 H), 6.65 – 6.59 (m, 1 H), 6.31 (dd, J = 6.0, 1.8 Hz, 1 H), 5.52 – 5.43 (m, 2 H), 5.38 – 5.27 (m, 2 H), 4.42 (s, 2 H), 3.85 (tt, J = 6.8, 4.8 Hz, 1 H), 3.80 (s, 3 H), 3.52 – 3.45 (m, 1 H), 3.42 (t, J = 6.5 Hz, 2 H), 2.54 (dddd, J = 14.5, 6.7, 4.2, 1.6 Hz, 1 H), 2.46 – 2.34 (m, 2 H), 2.31 – 2.15 (m, 4 H), 2.07 – 1.95 (m, 4 H), 1.63 – 1.54 (m, 2 H), 1.41 (tt, J = 10.0, 6.3 Hz, 2 H), 0.94 (t, J = 7.5 Hz, 3 H), 0.85 (s, 9 H), 0.04 (s, 3 H), 0.00 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.37, 161.67, 159.24, 139.25, 135.00, 134.16, 133.04, 132.60, 130.81, 129.31, 125.18, 124.49, 113.88, 72.68, 71.76, 70.02, 55.39, 43.51, 36.85, 35.76, 30.57, 29.54, 27.29, 26.31, 25.92, 20.88, 18.13, 14.32, -4.39, -4.53 ppm; HR-MS (ESI-TOF): calcd for C₃₄H₅₂O₄SiNa [M+Na]⁺: 575.3527, found: 575.3507.

(5Z,12E,15R,17Z)-15-Hydroxy-1-[(4-methoxybenzyl)oxy]prosta-5,9,12,17-tetraen-11-one (145): To



a stirred solution of dienone **144** (132 mg, 0.239 mmol, 1.0 equiv) in THF (4.4 mL) at 0 °C was added 3HF·Et₃N (900 μ L, 5.52 mmol, 23 equiv) dropwise. The resulting mixture was warmed to 25 °C and stirred for three

days. Upon completion of the reaction as indicated by thin-layer chromatography (TLC), the mixture was cooled to 0 °C, quenched with excess solid NaHCO₃, warmed to 25 °C and diluted with sat. aq. NaHCO₃-solution (10 mL). The aqueous layer was extracted with EtOAc (3×10 mL). The combined organic extracts were dried over Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:1) gave pure title compound (**145**, 92.7 mg, 0.210 mmol, 88 % yield) as a light yellow oil.

145: $R_f = 0.39$ (hexanes:EtOAc, 1:1); $[\alpha]_D^{25} = +133.8$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 3430$, 2933, 2859, 1699, 1651, 1513, 1247, 1097, 1036, 819 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.49 (ddd, J = 6.1, 2.6, 1.0 Hz, 1 H), 7.25 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.64 (dd, J = 9.1, 6.6 Hz, 1 H), 6.33 (dd, J = 5.9, 1.8 Hz, 1 H), 5.64 – 5.56 (m, 1 H), 5.51 – 5.44 (m, 1 H), 5.40 – 5.34 (m, 1 H), 5.34 – 5.28 (m, 1 H), 4.42 (s, 2 H), 3.84 – 3.78 (m, 1 H), 3.80 (s, 3 H), 3.56 – 3.50 (m, 1 H), 3.42 (t, J = 6.5 Hz, 2 H), 2.62 – 2.54 (m, 1 H), 2.48 (ddd, J = 15.1, 6.4, 4.8 Hz, 1 H), 2.45 – 2.40 (m, 1 H), 2.35 – 2.17 (m, 3 H), 2.10 – 2.03 (m, 2 H), 2.03 – 1.96 (m, 2 H), 1.85 (br s, 1 H), 1.63 – 1.55 (m, 2 H), 1.41 (tt, J = 7.5, 7.5 Hz, 2 H), 0.97 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.47, 161.95, 159.26, 139.76, 135.78, 134.96, 132.73, 131.93, 130.79, 129.35, 125.04, 123.92, 113.90, 72.70, 70.77, 70.00, 55.42, 43.50, 36.58, 35.26, 30.46, 29.54, 27.32, 26.32, 20.90, 14.35 ppm; HR-MS (ESI-TOF): calcd for C₂₈H₃₈O₄Na [M+Na]⁺: 461.2662, found: 461.2657.

(5Z,12E,15S,17Z)-15-Fluoro-1-[(4-methoxybenzyl)oxy]prosta-5,9,12,17-tetraen-11-one (146): To an



oven-dried flask was added potassium fluoride (34.0 mg, 0.593 mmol, 9.0 equiv) and the flask, along with the potassium fluoride, was flamedried under vacuum. After cooling to 25 °C, PhenoFluor [1,3-bis(2,6-

diisopropylphenyl)-2,2-difluoro-2,3-dihydro-1*H*-imidazole, 169 mg, 0.395 mmol, 6.0 equiv] was added, followed by a solution of hydroxydienone **67** (28.9 mg, 65.9 μ mol, 1.0 equiv) in anhydrous toluene (1.3 mL). *N*-Ethyldiisopropylamine (102 μ L, 593 μ mol, 9.0 equiv) was added and the reaction mixture was heated to 80 °C and stirred for 2.5 h. After cooling to 25 °C, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc:dichloromethane, 5:1:1) gave a mixture of the desired product and an elimination by-product. The mixture was further purified by preparative thin-layer

chromatography (SiO₂, hexanes:acetone, 6:1) to give the pure title compound (**146**, 10.0 mg, 22,7 μ mol, 35 % yield) as yellow oil.

146: $R_f = 0.27$ (hexanes: EtOAc, 4:1); $[\alpha]_D^{25} = +137.9$ (c = 0.80 in C_6H_6); IR (film): $v_{max} = 2933$, 2857, 1703, 1657, 1513, 1246, 1098, 1035, 820 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.50 (ddd, J = 6.1, 2.6, 1.0 Hz, 1 H), 7.25 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.59 (dd, J = 8.2, 6.8 Hz, 1 H), 6.33 (dd, J = 6.0, 1.8 Hz, 1 H), 5.60 – 5.53 (m, 1 H), 5.52 – 5.45 (m, 1 H), 5.40 – 5.34 (m, 1 H), 5.34 – 5.29 (m, 1 H), 4.65 (dtt, J = 47.9, 6.7, 5.3 Hz, 1 H), 4.42 (s, 2 H), 3.80 (s, 3 H), 3.51 – 3.45 (m, 1 H), 3.43 (t, J = 6.5 Hz, 2 H), 2.70 – 2.51 (m, 3 H), 2.51 – 2.36 (m, 2 H), 2.25 – 2.17 (m, 1 H), 2.08 – 1.96 (m, 4 H), 1.63 – 1.55 (m, 2 H), 1.46 – 1.38 (m, 2 H), 0.96 (t, J = 7.6 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.31, 161.92, 159.27, 139.94, 135.47, 134.95, 132.86, 130.83, 129.59 (d, J = 6.7 Hz), 129.35, 124.95, 122.21 (d, J = 6.3 Hz), 113.90, 92.15 (d, J = 174.3 Hz), 72.71, 70.02, 55.42, 43.42, 34.50 (d, J = 22.6 Hz), 32.75 (d, J = 21.4 Hz), 30.44, 29.54, 27.31, 26.31, 20.88, 14.21 ppm; HR-MS (ESI-TOF): calcd for C₂₈H₃₇FO₃Na [M+Na]⁺: 463.2619, found: 463.2618.

(5Z,12E,15S,17Z)-15-Fluoro-11-oxoprosta-5,9,12,17-tetraen-1-oic acid (38): To a stirred solution of fluorodienone 146 (10 mg, 23 μ mol, 1.0 equiv) in CH₃CN (90 μ L) and H₂O (10 μ L) at 25 °C was added 4-acetylamino-2,2,6,6tetramethyl-1-oxo-piperidinium tetrafluoroborate (16 mg, 140 μ mol,

6.0 equiv). After stirring at 25 °C for 35 min, the reaction mixture was diluted with water (2 mL). The aqueous layer was extracted with ether (3 \times 5 mL). The combined organic extracts were washed with brine (10 mL), dried over Na₂SO₄ and concentrated under reduced pressure. Purification by preparative thin layer chromatography (SiO₂, EtOAc) gave pure title compound (**28**, 3.4 mg, 10 µmol, 45 % yield) as a yellow oil.

38: $R_f = 0.27$ (EtOAc); $[\alpha]_D^{25} = +106.5$ (c = 0.2 in C_6H_6); IR (film): $v_{max} = 2926$, 1705, 1657, 1213, 1033 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.51 (ddd, J = 6.0, 2.6, 1.0 Hz, 1 H), 6.60 (t, J = 7.6 Hz, 1 H), 6.35 (dd, J = 6.0, 1.8 Hz, 1 H), 5.62 – 5.52 (m, 1 H), 5.52 – 5.44 (m, 1 H), 5.44 – 5.32 (m, 2 H), 4.67 (dtt, J = 47.9, 6.9, 5.3 Hz, 1 H), 3.56 - 3.45 (m, 1 H), 2.73 - 2.51 (m, 3 H), 2.51 - 2.38 (m, 2 H), 2.35 (t, J = 7.3 Hz, 2 H), 2.28 – 2.20 (m, 1 H), 2.10 – 2.01 (m, 4 H), 1.70 (tt, J = 7.4 Hz, 2 H), 0.97 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.31, 177.09, 161.75, 139.86, 135.51, 135.09, 131.60, 129.76 (d, J = 6.4 Hz), 126.03, 122.20 (d, J = 6.2 Hz), 92.21 (d,

J = 174.3 Hz), 43.31, 34.51 (d, J = 22.5 Hz), 32.98, 32.76 (d, J = 21.4 Hz), 30.39, 26.70, 24.53, 20.89, 14.21 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₇FO₃Na [M+Na]⁺: 357.1836, found: 357.1827.

Methyl (5Z,12E,15S,17Z)-15-fluoro-11-oxoprosta-5,9,12,17-tetraen-1-oate (39): To a stirred

COOMe COOMe F 39 solution of carboxylic acid **38** (2.5 mg, 7.5 μ mol, 1.0 equiv) in C₆H₆:MeOH (3:2, 0.35 mL) at 25 °C was added trimethylsilyl diazomethane (2.0 M in diethyl ether, 5.6 μ L, 11.2 μ mol, 1.5 equiv)

(yellow color persisted). After stirring at 25 °C for 35 min, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes:EtOAc, 4:1) to give the pure title compound (**39**, 1.3 mg, 3.7 μ mol, 50 % yield) as a light yellow oil.

39: $R_f = 0.45$ (hexanes: EtOAc, 2:1); $[\alpha]_D^{25} = +163.6$ (c = 0.18 in C_6H_6); IR (film): $v_{max} = 2926$, 1736, 1705, 1657, 1026 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.51 (dd, J = 6.1, 2.6 Hz, 1 H), 6.60 (t, J = 7.6 Hz, 1 H), 6.35 (d, J = 6.1 Hz, 1 H), 5.60 – 5.53 (m, 1 H), 5.51 – 5.44 (m, 1 H), 5.41 – 5.33 (m, 2 H), 4.66 (dtt, J = 48.0, 6.0, 6.0 Hz, 1 H), 3.66 (s, 3 H), 3.54 – 3.46 (m, 1 H), 2.71 – 2.52 (m, 3 H), 2.51 – 2.37 (m, 2 H), 2.30 (t, J = 7.4 Hz, 2 H), 2.27 – 2.19 (m, 1 H), 2.09 – 1.99 (m, 4 H), 1.68 (tt, J = 7.5, 7.5 Hz, 2 H), 0.97 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.28, 174.00, 161.76, 139.85, 135.49, 135.06, 131.78, 129.72 (d, J = 6.6 Hz), 125.83, 122.21 (d, J = 6.3 Hz), 92.16 (d, J = 174.4 Hz), 51.67, 43.32, 34.51 (d, J = 22.5 Hz), 33.51, 32.77 (d, J = 21.4 Hz), 30.37, 26.83, 24.80, 20.89, 14.22 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₂₉FO₃Na [M+Na]⁺: 371.1993, found: 371.2006.

Synthesis of Analogs 40 and 41:

1-(2-{[*tert*-Butyl(dimethyl)silyl]oxy}ethyl)cyclopent-2-en-1-ol (149): To a stirred solution of ethyl 2-(1-hydroxycyclopent-2-en-1-yl)acetate (147, 1.70 g, 10.0 mmol, 1.0 equiv) in THF (20 mL) at 0 °C was dropwise added lithium borohydride (2.0 M in THF, 10 mL, 20.0 mmol, 2.0 equiv). After stirring for 12 h at 25 °C, the clear solution was cooled to 0 °C, quenched by addition of sat. aq. NH4Cl-solution (10 mL) and allowed to warm to 25 °C. The resulting mixture was extracted with CH₂Cl₂ (3 × 30 mL), and the combined organic extracts were washed sequentially with H₂O (30 mL) and brine

(30 mL). The organic phase was dried (Na₂SO₄), filtered, and concentrated under reduced pressure to give crude diol, which was used directly in the next step without further purification.

To a stirred solution of crude diol in CH₂Cl₂ (15 mL) at 0 °C was added Et₃N (4.18 mL, 30.0 mmol, 3.0 equiv), DMAP (122 mg, 1.00 mmol, 0.1 equiv) and TBSCl (2.30 g, 15.0 mmol, 1.5 equiv). After stirring for 3 h at this temperature, the reaction mixture was quenched by addition of sat. aq. NH₄Cl-solution (15 mL), diluted with CH₂Cl₂ (50 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2×50 mL), and the combined organic extracts were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 10:1) gave pure title compound (**149**, 1.50 g, 6.20 mmol, 62 % yield for the two steps) as a colorless oil.

149: $R_f = 0.40$ (hexanes:EtOAc, 5:1); IR (film): $v_{max} = 3421$, 3055, 2954, 2857, 1541, 1472, 1360, 1254, 1084, 1033, 1006, 835, 775 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 5.84 (dt, J = 5.7, 2.3 Hz, 1 H), 5.78 (dt, J = 5.6, 2.1 Hz, 1 H), 3.95 (br s, 1 H), 3.90 – 3.88 (m, 2 H), 2.50 – 2.45 (m, 1 H), 2.27 – 2.21 (m, 1 H), 1.96 (ddd, J = 13.3, 8.4, 4.2 Hz, 1 H), 1.93 – 1.80 (m, 3 H), 0.89 (s, 9 H), 0.08 (s, 3 H), 0.08 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 136.21, 132.93, 85.78, 61.37, 41.31, 38.11, 30.85, 25.93, 18.15, -5.50 ppm; HR-MS (ESI-TOF): calcd for C₁₃H₂₆O₂SiNa [M+Na]⁺: 265.1599, found: 265.1589.

3-(2-{[*tert*-Butyl(dimethyl)silyl]oxy}ethyl)cyclopent-2-en-1-one (150): To a stirred solution of TBS ether 149 (560 mg, 2.15 mmol, 1.0 equiv) in CH₂Cl₂ (12 mL) at 25 °C was added NaIO₄-SiO₂ (6.00 g, 4.30 mmol, 2.0 equiv) and TEMPO (30.0 mg, 0.215 mmol, 0.1 equiv). After stirring for 4 h, the reaction mixture was filtered through Celite, washed with CH₂Cl₂ (50 mL) and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 3:1) gave pure title compound (150, 470 mg, 1.81 mmol, 84 % yield) as a colorless oil.

150: $R_f = 0.50$ (hexanes:EtOAc, 3:2); IR (film): $v_{max} = 2954$, 2928, 2857, 1709, 1674, 1617, 1472, 1255, 1094, 776 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 6.00 (s, 1 H), 3.84 (t, J = 6.2 Hz, 2 H), 2.63 – 2.61 (m, 4 H), 2.40 – 2.39 (m, 2 H), 0.87 (s, 9 H), 0.04 (s, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 210.37, 180.45, 130.75, 60.84, 36.82, 35.35, 32.12, 25.94, 18.32, -5.29, -5.30 ppm; HR-MS (ESI-TOF): calcd for C₁₃H₂₅O₂Si [M+H]⁺: 241.1618, found: 241.1622.

(5*E*)-3-(2-{[*tert*-Butyl(dimethyl)silyl]oxy}ethyl)-5-[(3*S*,5*Z*)-3-{[*tert*-butyl(dimethyl)silyl]oxy}oct-5-en-1-ylidene]cyclopent-2-en-1-one (152): To a stirred solution of diisopropylamine

TBSC (56 µL, 0.40 mmol, 2.0 equiv) in THF (2 mL) at 0 °C was dropwise added *n*-butyl lithium (1.6 M in hexanes, 240 µL; 0.39 mmol; 1.95 equiv.). After stirring for 20 min at this temperature, the clear solution was cooled to і Ōтвs 152 -78 °C and a solution of (R)-4-{2-[(t-butyldimethylsilyl)oxy]ethyl}cyclopent-2-enone (150) (50 mg, 0.20 mmol, 1.0 equiv) in THF (2 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 20 min at this temperature, a solution of aldehyde 58 (62 mg, 0.24 mmol, 1.2 equiv) in THF (2 mL) was added dropwise and stirring at this temperature was continued for an additional 30 min. The reaction mixture was then guenched by addition of sat. aq. NH₄Cl-solution (10 mL), diluted with EtOAc (10 mL), and allowed to warm to 25 °C. The phases were separated, the aq. layer was extracted with EtOAc (2×10 mL), and the combined organic extracts were washed with sat. brine (10 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product 151 was filtered through a short column (SiO₂, hexanes:EtOAc, 5:1) to obtain a mixture of diastereoisomers (ca. 3:1, 70 mg, 0.14 mmol, 70 % yield) as a colorless oil, which was used in the next step without further purification.

To a stirred solution of aldol product **151** (70 mg, 0.14 mmol, 1.0 equiv) in CH₂Cl₂ (2 mL) at 0 °C was added Et₃N (190 μ L, 1.4 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (54 μ L, 0.70 mmol, 5.0 equiv.). After stirring for 5 min at this temperature, the reaction mixture was quenched by addition of sat. aq. NaHCO₃-solution (10 mL), diluted with CH₂Cl₂ (10 mL), and allowed to warm to 25 °C. The phases were separated, the aq. layer was extracted with CH₂Cl₂ (2 × 10 mL), and the combined organic extracts were washed with H₂O (5 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude mesylate was filtered through a short column (SiO₂, hexanes:EtOAc, 4:1) to obtain a mixture of diastereoisomers (ca. 3:1, 74 mg, 0.129 mmol, 92 % yield) as a colorless oil, which was used in the next step without further purification.

To a vigorously stirred solution of above mesylate (74 mg, 0.13 mmol, 1.0 equiv) in CH₂Cl₂ (2 mL) at 25 °C was added Al₂O₃ (92 mg, 0.90 mmol, 7.0 equiv). After 2 h and 4 h time intervals two more portions of Al₂O₃ (2 × 92 mg, 2 × 0.90 mmol, 2 × 7.0 equiv) were added and vigorous stirring was continued for a total of 8 h. The resulting suspension was then filtered through Celite, washed with EtOAc, and the solution obtained was concentrated under reduced pressure. Flash

column chromatography (SiO₂, hexanes:EtOAc, 10:1) yielded pure title compound (**152**, 55 mg, 0.12 mmol, 89 % yield, 57 % yield for three steps) as a colorless oil.

152: $R_f = 0.73$ (hexanes:EtOAc, 3:1); $[\alpha]_D^{25} = +16.3$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 2955$, 2929, 2886, 2856, 1704, 1663, 1611, 1472, 1361, 1254, 1091 cm⁻¹; ¹H-NMR (500 MHz, C_6D_6) δ 6.85 – 6.75 (m, 1 H), 6.17 – 6.11 (m, 1 H), 5.55 – 5.39 (m, 2 H), 3.80 – 3.69 (m, 1 H), 3.48 (td, J = 6.3, 0.5 Hz, 2 H), 2.90 – 2.72 (m, 2 H), 2.32 – 2.14 (m, 6 H), 1.99 (ddt, J = 7.9, 7.3, 6.3 Hz, 2 H), 0.97 (s, 9 H), 0.93 (s, 9 H), 0.92 (t, J = 7.5 Hz, 3 H), 0.07 (d, J = 0.4 Hz, 3 H), 0.06 (d, J = 0.4 Hz, 3 H), -0.01 (s, 6 H) ppm; ¹³C-NMR (125 MHz, C_6D_6) δ 194.49, 170.62, 137.55, 133.92, 132.72, 129.85, 125.06, 71.94, 60.98, 37.60, 36.36, 35.84, 35.42, 26.08, 26.03, 21.15, 18.36, 18.27, 14.44, -4.38, -4.39, -5.32 ppm; HR-MS (ESI-TOF): calcd for $C_{27}H_{51}O_3Si_2$ [M+H]⁺: 479.3371, found: 479.3375.

(5*E*)-3-(2-Hydroxyethyl)-5-[(3*S*,5*Z*)-3-hydroxyoct-5-en-1-ylidene]cyclopent-2-en-1-one (40):

To a stirred solution of dienone **152** (30.0 mg, 62.6 μ mol, 1.0 equiv) in MeCN (0.6 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 124 μ L, ca. 3.10 mmol, ca. 50 equiv.) in MeCN (0.6 mL). After stirring for 1 h at this temperature, the reaction mixture was quenched by addition of sat. aq. NaHCO₃-solution (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with sat. brine (5 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure to a volume of ca. 0.1 mL (not to dryness!). Flash column chromatography (SiO₂, EtOAc) yielded pure title compound (**40**, 15.5 mg, 62.0 μ mol, 99 % yield) as a colorless oil.

40: $R_f = 0.25$ (EtOAc); $[\alpha]_D^{25} = +9.8$ (c = 1.0 in C_6H_6); IR (film): $v_{max} = 3372$, 2960, 2930, 1692, 1648, 1603, 1413, 1334, 1275, 1048 cm⁻¹; ¹H-NMR (500 MHz, C_6D_6) δ 6.80 (tt, J = 7.8, 1.7 Hz, 1 H), 6.22 (s, 1 H), 5.59 – 5.50 (m, 2 H), 4.00 (s, 2 H), 3.81 (quint, J = 6.1 Hz, 1 H), 3.69 (t, J = 6.1 Hz, 1 H), 2.96 (d, J = 21.2 Hz, 1 H), 2.82 (d, J = 21.2 Hz, 1 H), 2.43 – 2.23 (m, 6 H), 2.11 – 2.02 (m, 2 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (125 MHz, C_6D_6) δ 196.83, 174.27, 137.83, 134.27, 132.35, 131.51, 125.33, 70.85, 59.86, 37.50, 36.51, 35.72, 35.32, 21.19, 14.53 ppm; HR-MS (ESI-TOF): calcd for $C_{15}H_{22}O_3Na$ [M+Na]⁺: 273.1461, found: 273.1465.

(5E)-3-(2-{[tert-Butyl(dimethyl)silyl]oxy}ethyl)-5-[(2E,5Z)-octa-2,5-dien-1-ylidene]cyclo-

pent-2-en-1-one (154): To a stirred solution of diisopropylamine (130 µL, 0.92 mmol, 2.2 equiv)



in THF (12 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M in hexanes, 340 μ L, 0.84 mmol, 2.0 equiv). After stirring for 20 min at this temperature, the clear solution was cooled to -78 °C and a solution of enone

150 (100 mg, 0.42 mmol, 1.0 equiv) in THF (2 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 20 min at this temperature, a solution of aldehyde **64** (78 mg, 0.62 mmol, 1.5 equiv) in THF (8 mL) was added dropwise and stirring at this temperature was continued for an additional 30 min. The reaction mixture was then quenched with sat. aq. NH₄Cl-solution (75 mL), diluted with EtOAc (75 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with EtOAc (2×75 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product was filtered through a short column (SiO₂, hexanes:EtOAc, 3:1) to obtain a mixture of diastereoisomers as a colorless oil, which was taken to the next step without further purification.

To a stirred solution of the aldol product in CH₂Cl₂ (5 mL) at -10 °C was added DMAP (510 mg, 4.2 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (65 µL, 0.84 mmol, 2.0 equiv). After stirring for 30 min at this temperature, the reaction mixture was slowly warmed to 25 °C and stirred at this temperature for 6 h. The reaction mixture was quenched with saturated aqueous NaHCO₃-solution (5 mL) and diluted with CH₂Cl₂ (50 mL). The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 20 mL), and the combined organic extracts were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 7:1) gave pure title compound (**154**, 49 mg, 0.14 mmol, 34 % yield for the two steps) as a colorless oil. **154:** R_f = 0.69 (hexanes:EtOAc, 3:1); IR (film): $v_{max} = 2955$, 2929, 2856, 1702, 1662, 1257, 1091 cm⁻¹; ¹H-NMR (500 MHz, C₆D₆) δ 6.81 (ddt, *J* = 8.1, 7.3, 1.9 Hz, 1 H), 6.26 (ddd, *J* = 17.5, 0.8 Hz, 1 H), 5.02 - 4.92 (m, 1 H), 3.80 - 3.68 (m, 1 H), 3.02 - 2.76 (m, 2 H), 2.33 - 2.15 (m, 4 H), 2.04 - 1.91 (m, 2 H), 0.95 (s, 9 H), 0.89 (t, *J* = 7.5 Hz, 3 H), 0.05 (s, 3 H), 0.05 (s, 3 H) ppm; ¹³C-NMR (125 MHz, C₆D₆) δ 194.24, 163.95, 137.20, 133.96, 133.82, 133.11, 130.58, 125.00,

121.00, 71.92, 37.57, 35.84, 30.42, 26.04, 21.14, 18.25, 14.40, -4.41, -4.43 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₃₄O₂SiNa [M+Na]⁺: 369.2220, found: 369.2216.

(5*E*)-3-(2-Hydroxyethyl)-5-[(2*E*,5*Z*)-octa-2,5-dien-1-ylidene]cyclopent-2-en-1-one (41): To a stirred solution of TBS-protected trienone 154 (20.0 mg, 57.8 µmol, 1.0 equiv) in MeCN (2 mL) at 0 °C was dropwise added a solution of HF (50 % aq., 100 µL, ca. 2.89 mmol, ca. 50 equiv) in MeCN (1 mL). After stirring for 15 min at this temperature, the reaction mixture was quenched by addition of sat. brine (5 mL) and extracted with EtOAc (5 × 5 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated to a volume of ca. 1 mL (not to dryness!). Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 1:4) gave pure title compound (**41**, 11.5 mg, 50.2 µmol, 87 % yield) as a colorless oil.

41: $R_f = 0.74$ (EtOAc); IR (film): $v_{max} = 3419$, 2962, 2930, 1693, 1650, 1621, 1564, 1418, 1349, 1271, 1200, 1049 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 6.90 (d, J = 10.0 Hz, 1 H), 6.22 – 6.14 (m, 3 H), 5.53 – 5.49 (m, 1 H), 5.37 – 5.33 (m, 1 H), 3.92 (t, J = 6.3 Hz, 2 H), 3.24 (s, 3 H), 2.94 (t, J = 6.1 Hz, 2 H), 2.72 (t, J = 6.5 Hz, 2 H), 2.05 (quint, J = 7.2 Hz, 2 H), 0.97 (t, J = 7.6 Hz, 3 H) ppm; ¹³C-NMR (125 MHz, CDCl₃) δ 197.19, 171.39, 143.49, 133.95, 133.21, 132.83, 130.48, 126.32, 124.70, 60.31, 36.23, 35.39, 31.08, 20.67, 14.29 ppm; HR-MS (ESI-TOF): calcd for C₁₅H₂₁O₂ [M+H]⁺: 233.1536, found: 233.1538.

Cobalt alkyne complex 155a: To a stirred solution of alkyne 155 (1.38 g, 7.50 mmol, 1.0 equiv) TBSO Co₂(CO)₈ in CH₂Cl₂ (35 mL) at 0 °C was added Co₂(CO)₈ (2.50 g, 7.50 mmol, 1.0 equiv). The reaction mixture was slowly warmed to 25 °C and stirred at this temperature for 2 h. The resulting deep red solution was filtered through a pad of Celite, the filter cake was washed with Et₂O (100 mL), and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, pentane:Et₂O, 9:1) gave pure title compound (155a, 3.50 g, 7.50 mmol, quantitative yield).

155a: $R_f = 0.95$ (pentane:Et₂O, 9:1); IR (film): $v_{max} = 2957$, 2930, 2860, 2092, 2047, 1997, 1256, 1098, 834 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 5.94 (s, 1 H), 3.75 (t, J = 7.0 Hz, 2 H), 2.97 (d, J = 7.0 Hz, 2 H), 0.83 (s, 9 H), 0.00 (s, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 199.93, 92.39, 73.65, 63.59, 37.16, 25.91, 18.33, -5.38 ppm.

2-(2-{[*tert*-Butyl(dimethyl)silyl]oxy}ethyl)cyclopent-2-en-1-one (157): To a stirred solution of TBSO Cobalt alkyne complex 155a (1.10 g, 3.10 mmol, 1.0 equiv) at 25 °C in vinyl benzoate (20.0 mL, 202 mmol, 65 equiv) was added a solution of NMO·H₂O (2.50 g, 18.9 mmol, 6.1 equiv) in CH₂Cl₂ (35 mL) via addition funnel over 1 h.

After stirring for 15 h at this temperature the crude reaction mixture was filtered through a short column (SiO₂, Et₂O) and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:Et₂O, 9.5:0.5 \rightarrow 7:3) gave pure title compound (**157**, 0.460 g, 1.91 mmol, 62 % yield).

157: $R_f = 0.17$ (hexanes:Et₂O, 9:1); IR (film): $v_{max} = 2954$, 2928, 2856, 1703, 1251, 1098 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.44 – 7.37 (m, 1 H), 3.69 (t, J = 6.4 Hz, 2 H), 2.55 (dq, J = 4.5, 2.2 Hz, 2 H), 2.37 (ddd, J = 12.3, 5.8, 3.8 Hz, 4 H), 0.85 (s, 9 H), 0.00 (s, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 209.85, 159.42, 143.28, 61.04, 34.36, 28.34, 26.65, 25.88, 18.25, -5.34 ppm; HR-MS (ESI-TOF): calcd for C₁₃H₂₅O₂Si [M+H]⁺: 241.1618, found: 241.1607.

(5*E*)-2-(2-Hydroxyethyl)-5-[(3*S*,5*Z*)-3-hydroxyoct-5-en-1-ylidene]cyclopent-2-en-1-one (42):

^{H0} \downarrow_{42} ^{H0} To a stirred solution of diisopropylamine (0.13 mL, 0.98 mmol, 1.3 equiv) in THF (8 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M in hexanes, 0.33 mL, 0.83 mmol, 1.1 equiv). After stirring for 20 min at this temperature, the clear solution was cooled to -78 °C and a solution of enone **157** (0.18 g, 0.77 mmol, 1.0 equiv) in THF (2 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 20 min at this temperature, a solution of aldehyde **58** (0.19 g, 0.77 mmol, 1.0 equiv) in THF (2 mL) was added dropwise and stirring at this temperature was continued for an additional 30 min. The reaction mixture was then quenched by addition of sat. aq. NH₄Cl-solution (20 mL), diluted with Et₂O (20 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with Et₂O (2 × 25 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product was taken to the next step without further purification.

To a stirred solution of aldol product (0.38 g, 0.77 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added Et_3N (1.0 mL, 7.7 mmol, 10 equiv), and then, slowly and dropwise, methanesulfonyl chloride (0.29 mL, 3.9 mmol, 5.0 equiv). After stirring for 2 h at 25 °C, the

reaction mixture was quenched by addition of H_2O (20 mL) and diluted with CH_2Cl_2 (20 mL). The phases were separated, the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL), and the combined organic extracts were washed with H_2O (20 mL), dried (Na₂SO₄), filtered, and concentrated. The crude mesylate was taken to the next step without further purification.

To a vigorously stirred solution of above mesylate (0.44 g, 0.77 mmol, 1.0 equiv) in CH_2Cl_2 (25 mL) at 25 °C was added Al_2O_3 (0.78 g, 7.7 mmol, 10 equiv). After 16 h the resulting suspension was then filtered through Celite, washed with EtOAc, and the filtrate was concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 8.5:1.5) gave pure TBS protected intermediate **159** (0.15 g, 0.31 mmol 40% yield for the three steps) as a light yellow oil.

To a stirred solution of above TBS protected intermediate **159** (66 mg, 0.13 mmol, 1.0 equiv) in MeCN (1.5 mL) at 0 °C was added dropwise HF (50 % aq., 0.14 mL, 4.1 mmol, 30 equiv). After stirring for 30 min at this temperature, the reaction mixture was quenched by addition of sat. brine (5 mL) and diluted with EtOAc (10 mL). The phases were separated and the aqueous layer was extracted with EtOAc (3×5 mL), and the combined organic extracts were washed with saturated aqueous NaHCO₃-solution (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 8:2) gave pure title compound (**42**, 13 mg, 0.051 mmol, 38 % yield) as a colorless oil.

42: $R_f = 0.70$ (hexanes: EtOAc, 9:1), $[\alpha]_D^{25} = -3.53$ (c = 0.34 in CHCl₃); IR (film): $v_{max} = 2947$, 2921, 1727, 1546, 1343, 1272, 1169 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.34 (s, 1 H), 6.73 (t, J = 7.8 Hz, 1 H), 5.66 – 5.54 (m, 1 H), 5.44 – 5.32 (m, 1 H), 3.93 – 3.81 (m, 1 H), 3.78 (t, J = 5.8 Hz, 2 H), 3.23 – 3.13 (m, 2 H), 2.59 (t, J = 6.0 Hz, 2 H), 2.44 (q, J = 7.5, 6.7 Hz, 2 H), 2.29 (quint, J = 7.9 Hz, 2 H), 2.14 – 2.01 (m, 2 H), 0.99 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.84, 152.83, 145.81, 136.74, 135.68, 132.36, 123.74, 70.49, 61.21, 36.90, 35.05, 30.71, 30.05, 20.76, 14.20 ppm; HR-MS (ESI-TOF): calcd for C₁₅H₂₂O₃Na [M+Na]⁺: 273.1461, found: 273.1452.

$(5E) - 2 - (2 - \{[tert-Butyl(dimethyl)silyl]oxy\} ethyl) - 5 - [(2E,5Z) - octa - 2,5 - dien - 1 - ylidene]cyclo-line - 1$

pent-2-en-1-one (161): To a stirred solution of diisopropylamine (0.28 mL, 2.1 mmol, 1.3 equiv)



in THF (16 mL) at 0 °C was dropwise added *n*-butyl lithium (2.5 M in hexanes, 0.69 mL, 1.7 mmol, 1.1 equiv). After stirring for 20 min at this temperature, the clear solution was cooled to -78 °C and a solution

of enone **157** (0.38 g, 1.6 mmol, 1.0 equiv) in THF (4 mL) was added dropwise. After stirring the resulting slightly yellow solution for an additional 20 min at this temperature, a solution of aldehyde **64** (200 mg, 1.6 mmol, 1.0 equiv) in THF (2 mL) was added dropwise and stirring at this temperature was continued for an additional 30 min. The reaction mixture was then quenched by addition of sat. aq. NH₄Cl-solution (20 mL), diluted with Et₂O (20 mL), and allowed to warm to 25 °C. The phases were separated, the aqueous layer was extracted with Et₂O (2×25 mL), and the combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude aldol product was taken to the next step without further purification.

To a stirred solution of aldol product (0.58 g, 1.6 mmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at 0 °C was added Et₃N (0.50 mL, 3.5 mmol, 2.2 equiv), and then, slowly and dropwise, methanesulfonyl chloride (0.13 mL, 1.8 mmol, 1.1 equiv). After stirring for 2 h at 25 °C, the reaction mixture was quenched with H₂O (20 mL) and diluted with CH₂Cl₂ (20 mL). The phases were separated, the aqueous layer was extracted with CH₂Cl₂ (2 × 20 mL), and the combined organic extracts were washed with H₂O (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude mesylate was taken to the next step without further purification.

To a vigorously stirred solution of above mesylate (0.71 g, 1.6 mmol, 1.0 equiv) in CH₂Cl₂ (25 mL) at 25 °C was added Al₂O₃ (1.6 g, 16 mmol, 10 equiv). After 16 h the resulting suspension was filtered through Celite, washed with EtOAc, and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 8.5:1.5) gave pure title compound (**161**, 130 mg, 0.31 mmol, 23 % yield for the three steps) as a light yellow oil. **161:** R_f =0.78 (hexanes:EtOAc, 8:2); IR (film): v_{max} =3012, 2955, 2927, 2855, 1689, 1638, 1627, 1253, 1093, 831 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.25 (m, 1 H), 6.95 (d, *J*=10.8 Hz, 1 H), 6.26 – 6.12 (m, 2 H), 5.56 – 5.44 (m, 1 H), 5.42 – 5.27 (m, 1 H), 3.79 – 3.68 (m, 2 H), 3.18 – 3.11 (m, 2 H), 2.94 (t, *J*=6.7 Hz, 2 H), 2.48 (t, *J*=6.4 Hz, 2 H), 2.10 – 1.97 (m, 2 H), 1.03 – 0.92 (m, 3 H), 0.86 – 0.85 (m, 9 H), 0.00 (s, 6 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 196.62, 150.74, 145.43, 143.21, 133.75, 132.73, 131.00, 126.36, 124.62, 61.03, 30.98, 30.56, 29.06, 25.88, 20.55, 18.23, 14.16, -5.35 ppm; HR-MS (ESI-TOF): calcd for C₂₁H₃₄O₂SiNa [M+Na]⁺: 369.2220, found: 369.2223.

(5E)-2-(2-Hydroxyethyl)-5-[(2E,5Z)-octa-2,5-dien-1-ylidene]cyclopent-2-en-1-one (43): To a

HO

$$43$$
 stirred solution of TBS protected analog **95** (15 mg, 43 µmol, 1.0 equiv)
in MeCN (0.5 mL) at 0 °C was dropwise added HF (50 % aq., 0.040 mL,

1.3 mmol, 30 equiv). After stirring for 30 min at this temperature the reaction mixture was then quenched by addition of sat. brine (5 mL) and diluted with EtOAc (10 mL). The phases were separated and the aqueous layer was extracted with EtOAc (3×5 mL), and the combined organic extracts were washed with sat. aq. NaHCO₃-solution (20 mL), dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, hexanes:EtOAc, 8:2) gave pure title compound (**43**, 7.0 mg, 30 µmol, 70 % yield) as a colorless oil.

43: $R_f = 0.60$ (EtOAc); IR (film): $v_{max} = 3405$, 2962, 2930, 2874, 1776, 1679, 1624, 1046 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 7.23 (s, 1 H), 6.97 (d, J = 8.5 Hz, 1 H), 6.23 – 6.13 (m, 2 H), 5.48 (q, J = 7.8 Hz, 1 H), 5.38 – 5.27 (m, 1 H), 3.72 (t, J = 5.8 Hz, 2 H), 3.20 – 3.10 (m, 2 H), 2.92 (t, J = 5.7 Hz, 2 H), 2.54 (t, J = 5.9 Hz, 2 H), 2.02 (quint, J = 7.4 Hz, 2 H), 0.93 (t, J = 7.5 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 197.84, 151.74, 146.36, 144.25, 133.94, 132.52, 132.16, 126.19, 124.46, 61.36, 31.05, 30.76, 30.29, 20.58, 14.18 ppm; HR-MS (ESI-TOF): calcd for C₁₅H₂₀O₂Na [M+Na]⁺: 255.1356, found: 255.1365.

Synthesis of Δ^{12} -PGJ₂ Lactone (44):

(3S)-3-{[tert-Butyl(dimethyl)silyl]oxy}octan-1-ol (162): To a vigorously stirred solution of



alkyne **86** (0.600 mg, 2.23 mmol, 1.0 equiv) in MeOH (8 mL) was added Pd-C (10% Pd on carbon, 60.0 mg, 10 wt%) at 25 °C. The suspension was degassed and purged with Ar three times, then the atmosphere was

exchanged to H_2 (balloon). After vigorous stirring for 24 h at the same temperature, the reaction mixture was filtered through Celite, washed with EtOAc, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 4:1) yielded pure title compound (338 mg, 1.39 mmol, 63 % yield) as a colorless oil.

162: $R_f = 0.50$ (hexanes: EtOAc, 4:1); $[\alpha]_D^{25} = +11.7$ (c = 2.1, C_6H_6); FT-IR (neat): $v_{max} = 3363$, 2955, 2930, 2858, 1601, 1471, 1463, 1378, 1256, 1058, 1005, 835, 774 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 3.93 – 3.89 (m, 1 H), 3.87 – 3.82 (m, 1 H), 3.71 (dt, J = 10.8, 5.4 Hz, 1 H), 2.44 (s, 1 H), 1.85 – 1.79 (m, 1 H), 1.67 – 1.62 (m, 1 H), 1.54 – 1.50 (m, 2 H), 1.32 – 1.24 (s, 6 H), 0.89 – 0.88

(m, 12 H), 0.09 (s, 3 H), 0.08 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 72.12, 60.41, 37.73, 36.87, 32.04, 25.92, 25.11, 22.70, 18.06, 14.09, -4.33, -4.63 ppm; HR-MS (ESI) calcd for C₁₄H₃₃O₂Si [M+H]⁺: 261.2244, found: 261.2231.

(3*S*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}octanal (163): To a solution of primary alcohol 162 $\stackrel{\text{H}}{\longrightarrow} \stackrel{\text{Me}}{\longrightarrow}$ (600 mg, 2.30 mmol, 1.0 equiv) in CH₂Cl₂ (20 mL) at 0 °C was added Dess-163 Martin periodinane (1.95 g, 4.60 mmol, 2.0 equiv). The reaction mixture was warmed to 25 °C and stirred for 90 min. The reaction was then quenched by addition of sat. aq. Na₂S₂O₃ (4 mL) and sat. aq. NaHCO₃ (4 mL) and stirred for 10 min. The layers were separated, and the aqueous phase was extracted with CH₂Cl₂ (10 mL). The combined organic extracts were dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes: EtOAc, 19:1→9:1) yielded the title aldehyde (498 mg, 1.93 mmol, 84% yield) as a colorless oil.

163: $R_f = 0.60$ (hexanes:EtOAc, 10:1); $[\alpha]_D^{25} = -6.1$ (c = 1.0, CHCl₃); FT-IR (neat): $v_{max} = 2956$, 2929, 2858, 1727, 1471, 1361, 1254, 1100, 1053, 1005, 835, 774 cm⁻¹; ¹H-NMR (600 MHz, CDCl₃) δ 9.81 (t, J = 2.5 Hz, 1 H), 4.18 (quint, J = 5.9 Hz, 1 H), 2.52 – 2.45 (m, 2 H), 1.58 – 1.47 (m, 2 H), 1.36 – 1.22 (m, 6 H), 0.90 – 0.87 (m, 12 H), 0.07 (s, 3 H), 0.06 (s, 3 H) ppm; ¹³C-NMR (151 MHz, CDCl₃) δ 202.60, 68.40, 50.92, 37.91, 31.87, 25.86, 24.90, 22.67, 18.09, 14.08, -4.32, -4.59 ppm; HR-MS (ESI) calcd for C₁₄H₃₀O₂SiNa [M+Na]⁺: 281.1907, found: 281.1909.

(5Z,12E,15S)-1,15-Epoxyprosta-5,9,12-triene-1,11-dione (44): To a stirred solution of 2-methyl-6-nitrobenzoic anhydride (11 mg, 31 µmol, 2.0 equiv) and 4-dimethylaminopyridine (10 mg, 91 µmol, 6.0 equiv) in CH₂Cl₂ (10 mL) was added a solution of Δ^{12} -PGJ₂ (164)⁷ (5.0 mg, 15 µmol, 1.0 equiv) in CH₂Cl₂ (5 mL) at 25 °C dropwise via syringe pump over 15 h. After stirring for an additional 2 h, the reaction mixture was washed sequentially with sat. aq. NaHCO₃-solution (10 mL), aq. HCl (0.2 M, 10 mL), and sat. brine (10 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Flash column chromatography (SiO₂, hexanes:EtOAc, 3:1) gave pure title compound (3.4 mg, 11 µmol, 72 % yield) as a colorless oil.

44: $R_f = 0.40$ (hexanes:EtOAc, 7:3); $[\alpha]_D^{25} = +26.4$ (c = 0.3 in C₆H₆); IR (film): $v_{max} = 2930$, 2859, 1727, 1704, 1655, 1581, 1456, 1328, 1243, 1151, 1048, 833 cm⁻¹; ¹H-NMR (600 MHz, C₆D₆) δ

6.78 (ddd, J = 6.1, 2.6, 0.9 Hz, 1 H), 6.66 (ddt, J = 11.4, 4.8, 1.3 Hz, 1 H), 6.20 (dd, J = 6.1, 1.9 Hz, 1 H), 5.20 – 5.08 (m, 3 H), 3.22 – 3.20 (m, 1 H), 2.43 (ddd, J = 14.5, 9.2, 5.7 Hz, 1 H), 2.37 – 2.31 (m, 1 H), 2.26 (ddd, J = 15.1, 11.4, 9.5 Hz, 1 H), 2.15 – 2.07 (m, 2 H), 2.04 – 1.96 (m, 2 H), 1.86 – 1.81 (m, 1 H), 1.56 – 1.46 (m, 1 H), 1.41 – 1.08 (m, 9 H), 0.87 (t, J = 7.2 Hz, 3 H) ppm; ¹³C-NMR (151 MHz, C₆D₆) δ 194.69, 172.42, 159.56, 140.28, 135.60, 131.83, 130.91, 125.53, 73.20, 43.47, 34.40, 34.14, 32.75, 31.90, 28.45, 26.06, 25.51, 24.64, 22.92, 14.22 ppm; HR-MS (ESI-TOF): calcd for C₂₀H₂₈O₃Na [M+Na]⁺: 339.1931, found: 339.1925.

IV. Biological Evaluation

(a) Nuclear Export Studies

Material and Methods

Cell culture, transfection, immunofluorescent staining and microscopy

Cell lines were maintained as recommended by the American Type Culture Collection in DMEM containing 5 % glutamine (Thermo Fisher Scientific, Waltham, USA) supplemented with 10 % FBS (Thermo Fisher Scientific, Waltham, USA). For treatment or transfections, cells were seeded at a density of $0.2 \cdot 10^5$ cells/well in 8 well microscopy chambers (Ibidi GmbH, Martinsried, Germany). On the following day transfection with jetPRIME[®] (Polyplus transfection, Illkirch, France) was performed according to the manufacturers protocol. For immunofluorescent staining, cells were fixed in 4 % PFA for 10 min and permeabilized with 0.1 % Triton X-100 in PBS for 5 min. Antibodies were diluted in PBS containing 1 % FBS and applied for 1 h to the cells. Nuclei were labeled by incubating for 10 min with Hoechst 33342 (10 µg/ml in PBS). 24 h after transfection or after immunofluorescent staining, cells were imaged using a Nikon Eclipse Ti confocal spinning disc microscope. Brightness and contrast of the images have been adapted using the software CanvasTM (ACD Systems, Seattle, USA) for optimal visibility.

Plasmids and antibodies

pC3_TFIIA_GFP was a kind gift from Prof. Dr. Stauber (Mainz, Germany). pC3_Crm1_GFP/_HA, pC3_Crm1_{C5285}_GFP/_HA and pC3_HIV-1 Rev_BFP were described in the literature.⁸ Anti-HA was obtained from BioLegend[®] (SanDiego, USA) and anti-mouse IgG labeled with Alexa Fluor[®]647 from Cell Signaling Technologies (Cambridge, UK).

Cellular treatment

Compounds 2, 11, 21 and 27 were dissolved in DMSO at a stock concentration of 50 mM and were added to the cell medium at a final concentration of 50 μ M. Dithiothreitol (DTT) was dissolved at 1 M stock concentration in water and sterile filtered. For co-treatment, DTT was added at a final concentration of 1 mM before addition of compounds.

Peptides and MS

Peptides were obtained from the peptide synthesis platform of the Helmholtz Centre for Infection research (Dr. W. Tegge). The C-peptide represents the amino acid sequence 523-531 of wildtype Crm1 (DLLGL<u>C</u>EQK, C-peptide). In the S-peptide the Cys528 of Crm1 was exchanged to serine (DLLGL<u>S</u>EQK). Peptides were dissolved at a concentration of 100 μ M in water (pH 8.4). Each compound was added at a concentration of 50 μ M, and samples were incubated at room temperature for 1 h while shaking. Afterwards samples were diluted 1:10 in water and analysis was performed using a UPLC-ESI-Q-TOF-MS that consisted of an UltiMate 3000 (Thermo Fisher

Scientific, Waltham, USA) coupled to maxisIITM HD mass spectrometer (Bruker Daltonic, Billerica, USA).

<u>Results</u>

Export inhibition monitored by the translocation biosensor

For detecting Crm1 dependent nuclear export inhibition HeLa cells stably expressing a fluorescent translocation biosensor (HeLa_{RevBio})⁹ were challenged with compounds **2**, **11**, **21**, and **27**. The translocation biosensor is a fusion protein consisting of a nuclear localization signal (SV40-NLS), glutathione S-transferase (GST), green fluorescent protein (GFP) and a nuclear export signal (HIV1-RevNES). GST is included to avoid passive diffusion and GFP allows for detection by fluorescence microscopy. Due to the two transport signals (NLS/NES), the biosensor is permanently shuttling between nucleus and cytoplasm.¹⁰ Owing to the comparatively stronger NES, the GFP signal is mainly localized in the cytoplasm of untreated cells. Upon addition of an export inhibitor, the GFP-signal accumulates in the nucleus. For all compounds as well as the positive control ratjadone A (RatA), a nuclear accumulation of the biosensor was detected indicating export inhibition.



Figure S1: 2, 11, 21, and 27 inhibited nuclear export of a fluorescent translocation biosensor.

HeLa_{RevBio} were treated with the compounds (50 μ M) and imaged after 60 min of incubation under live cell conditions. Upper row: GFP-signal; lower row: Merge with bright field image and depiction of the cellular borders (dotted lines).

DTT disabled export inhibitory effect of 2, 11, 21, and 27

In order to assess whether inhibition occurred through the modification of a cysteine residue, as formerly described for other inhibitors of nuclear export,¹¹ DTT was added prior to incubation of $HeLa_{RevBio}$ with the compounds. In all cases, DTT was able to preserve the cytoplasmic biosensor localization. Thus the inhibitory mechanism seems to comprise a nucleophilic attack by a thiol.



Figure S2: DTT disables export inhibition by the compounds.

DTT (1 mM) was added to HeLa_{RevBio} cells prior to treatment with the compounds (50 μ M) for 1 h. Cells were imaged under live cell conditions. Upper row GFP-signal, lower row merge with bright field image and depiction of the cellular borders (dotted lines).

Compounds bind to Cys528 of Crm1

Cys528 of Crm1 is located in the NES-binding pocket and is the target of formerly described nuclear export inhibitors like leptomycin B and ratjadones.¹¹ To investigate whether the compounds also act through binding to Cys528, a peptide was generated comprising residues 523–531 of Crm1 (DLLGL<u>C</u>EQK). This peptide was incubated with the compounds and then subjected to mass spectrometric analysis. As a control, a peptide containing a cysteine to serine exchange was included (DLLGL<u>S</u>EQK). Table ST1 gives an overview about the masses of the peptides and compounds as well as the expected masses of peptide-compound conjugates.

Peptide	Compound	Molecular weight [g/mol]	Exact mass [g/mol]	Exact mass for Peptide + comp. [g/mol]	m/z for [M+2H] ²⁺
DLLGL <u>C</u> EQK	C-peptide	1018.1950	1017.5165		509.7655
	2	346.4670	346.2144	1363.7309	682.8727
	11	314.4250	314.1882	1331.7047	666.8596
	21	368.3962	368.1599	1385.6764	693.8455
	27	418.4562	418.1756	1435.6921	718.8533
DLLGL <u>S</u> EQK	S-peptide	1002.1340	1001.5393		501.7769
	2	346.4670	346.2144	1347.7537	674.8841
	11	314.4250	314.1882	1315.7275	658.8710
	21	368.3962	368.1599	1369.6993	685.8569
	27	418.4562	418.1756	1419.7149	710.8647

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I ADIE NI I' WIASSES	or nennaes ana	nentiae-compolina	conmostes
	or peptites and	pepulae compound	conjugates

The doubly charged ion was the most abundant in the mass spectra. Its m/z values are therefore shown in the last column of ST1 as well as in the following chromatograms. Figure S3 depicts the chromatogram over the full analysis time range. Extracted ion chromatograms (EIC) are shown for the C-peptide with the mass of twofold charged C-peptide ions and the expected mass of the conjugate of C-peptide with compound **11** (a,b), C-peptide after incubation with compound **11** with the expected mass of the conjugate ion (c), and the S-peptide with the mass of its twofold charged ion and the expected mass of the conjugate with compound **11** (d,e). Only for the C-peptide a signal originating from the conjugate with compound **11** was detected (c).



Figure S3: Compound 11 binds to Cys528 of Crm1

Wildtype Crm1 and cysteine mutant Crm1 representing peptides (both 100 μ M) were incubated with compound **11** (50 μ M) for 1 h. By mass spectrometry the formation of peptide-compound conjugates was analyzed. EIC of C-peptide without (a,b) or with compound **11** (c) and the S-peptide without (d) or with compound **11** (e) are shown. Only for C-peptide and compound **11** a conjugate derived signal was obtained (C). On the right the isotopic mass pattern of the respective peaks is depicted.

For all compounds (2, 11, 21, and 27) the formation of C-peptide-compound conjugate was verified using this approach. In figure S4 the EIC of the twofold charged conjugate ions are depicted. The respective masses are shown in figure S5. In all cases there was no conjugate ion detectable for the compounds with the S-peptide (data not shown). The corresponding total ion chromatograms (TIC) are included in figure S6.



Figure S4: EIC of the conjugates of C-peptide with compounds 2, 11, 21 or 27

C-peptide (100 μ M) was incubated with compound **2**, **11**, **21** or **27** (50 μ M) for 1 h and subjected for mass spectrometric analysis. EIC for the expected twofold charged conjugate ions are shown.



Figure S5: Mass spectra of the C-peptide compound conjugates



Figure S6: TIC of all peptide/peptide-compound samples

Inhibition of nuclear export depends on Cys528 of Crm1

In order to validate the compound binding to Cys528 of Crm1 in the cellular environment, their effect on the co-localization of Crm1 or mutant Crm1_{C5285} with HIV-1 Rev was assessed. The HIV-1 Rev protein binds to partially or unspliced HIV-1 RNA and mediates nuclear export via interaction with Crm1. This interaction is based on the HIV-1 NES binding to the NES-binding pocket on Crm1.¹² The interaction is sensitive to binding of inhibitors to Cys528 of Crm1.⁸ To monitor the compounds effect on this interaction, wildtype Crm1 or mutant Crm1_{C5285} was expressed as fusion to GFP together with HIV-1 Rev fused to BFP and their intracellular localization was analyzed using confocal microscopy. When only Crm1- or Crm1_{C5285}-GFP are expressed, a prominent signal of the nuclear membrane was detected as well as a weak cytoplasmic and nuclear distribution. Upon co-expression with HIV-1 Rev-BFP, Crm1- or Crm1_{C5285}-GFP were additionally localized at the nucleoli due to the strong interaction between the two proteins. Upon incubation with the compounds, the co-localization of Crm1-GFP with HIV-1 Rev-BFP was decreased. In contrast, no effect was observed on the co-localization of Crm1_{C5285}-GFP with HIV-1 Rev-BFP, indicating that the inhibition occurs through a modification of Cys528.



Figure S7: Co-localization of Crm1 and HIV-1 Rev is disabled by the compounds

HeLa cells were co-transfected with plasmids encoding for Crm1-GFP and HIV-1 Rev-BFP or Crm1_{C5288}-GFP and HIV-1 Rev-BFP.⁸ The day after transfection compounds **2**, **11**, **21**, and **27** were applied at a concentration of 50 μ M for 1.5 h. Cells were fixed and the localization of fluorescent signals was analyzed by confocal microscopy.

Rescue of translocation biosensor nuclear export by Crm1_{C5285}-HA

To further validate whether the compounds inactivate Crm1 by binding to Cys528, we tested whether expression of the Cys528 to Ser mutant of Crm1 can rescue the nuclear export of the translocation biosensor under compound treatment. Crm1 or Crm1_{C5285} were expressed as

N-terminal fusions to HA in HeLa_{RevBio} cells. The day after transfection compound **2** was applied at a concentration of 50 μ M for 1.5 h. Cells were fixed and Crm1-/Crm1_{C5285}–HA was immunofluorescently labeled with antibodies specific to HA and mouse-IgG coupled to ALX647. Cells expressing Crm1/Crm1_{C5285} were analyzed for the localization of the translocation biosensor. Crm1_{C5285}–HA but not Crm1-HA was found to circumvent the export inhibitory effect of compound **2**, as shown by the cytoplasmic localization of the translocation biosensor.



Figure S8: Expression of Crm1_{C5285} rescues nuclear export of the translocation biosensor

HeLa_{RevBio} cells were transfected with plasmids encoding for Crm1- or Crm1_{C528S}-HA. The day after transfection compound **2** was applied at a concentration of 50 μ M for 1.5 h. Cells were fixed and the localization of fluorescent signals was analyzed by confocal microscopy.

IV. (b) i) NCI-60 Data of Tested Compounds

Developmental Ther	apeutics Program	NSC: D-782132 / 1	Conc: 1.00E-5 Molar	Test Date: Sep 29, 2014	
One Dose Mea	an Graph	Experiment ID: 1409	Report Date: Dec 27, 2015		
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Perc	cent	
Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer A549/ATCC EKVX HOP-62 HOP-92 NCI-H23 NCI-H322M NCI-H322M NCI-H322M NCI-H322M NCI-H322M NCI-H322M NCI-H322M NCI-H322M Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251 Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-ME-2 SK-ME-2 SK-ME-2 SK-ME-2 SK-ME-2 SK-ME-2 SK-ME-2 SK-ME-2 SK-ME-2 SK-ME-2	4.11 75.18 17.09 5.70 10.11 10.28 75.90 104.54 96.86 75.23 83.12 79.89 85.65 64.80 -10.69 65.39 57.72 8.90 74.61 47.86 41.58 49.60 81.31 95.95 59.20 65.04 88.87 3.29 17.40 67.53 57.77 36.88 62.16 54.41 60.27 55.18 27.67 99.23 14.82 74.77 128.27 19.99 78.31 15.72 68.54 90.88 84.51 83.91 94.25 46.21 12.01 <	100 50			
	150	100 50	0 -50	-100 -150	

	National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results															
NSC : D - 782	133 / 1				Experiment ID : 1410NS77							Test 1	Гуре : 08	Units : N	Units : Molar	
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Octob	er 27, 20	14			QNS	:	MC :		
COMI : KCN-F	PGJ-4				Sta	in Rea	gent : S	RB Dual-	Pass I	Related		SSPL	: 0ZAS			
						Log10 Concentration										
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	n Optica -6.0	I Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	rowth -5.0	-4.0	GI50	TGI	LC50	
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.340 0.973 0.334 0.644 0.758 0.284	1.545 3.240 2.639 2.337 2.788 1.650	1.500 3.206 2.604 2.348 2.723 1.489	1.526 3.201 2.653 2.299 2.796 1.525	0.495 2.554 1.304 1.470 1.775 0.603	0.356 0.853 0.441 0.497 0.744 0.267	0.270 0.553 0.304 0.456 0.532 0.226	96 98 98 101 97 88	98 98 101 98 100 91	13 70 42 49 50 23	1 -12 5 -23 -2 -6	-21 -43 -9 -29 -30 -21	3.68E-7 1.74E-6 7.32E-7 9.45E-7 1.00E-6 4.03E-7	1.14E-5 7.07E-6 2.17E-5 4.80E-6 9.21E-6 6.18E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4	
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H420 NCI-H460 NCI-H522	Cancer 0.444 0.724 0.644 1.250 1.157 0.578 1.071 0.190 1.254	1.644 1.857 1.687 1.810 2.429 1.891 2.481 2.141 2.501	1.588 1.794 1.678 1.721 2.491 1.855 2.418 2.173 2.420	1.598 1.720 1.614 1.762 2.394 1.847 2.408 2.207 2.415	1.651 1.728 1.331 1.860 2.444 1.645 2.311 2.151 1.898	0.385 0.840 0.472 1.160 0.568 0.301 1.105 0.232 0.220	0.071 0.009 0.139 0.037 0.501 0.065 0.068 0.113 0.074	95 94 99 84 105 97 96 102 93	96 88 93 91 97 97 95 103 93	101 89 66 109 101 81 88 100 52	-13 10 -27 -7 -51 -48 2 2 -82	-84 -99 -78 -97 -57 -89 -94 -41 -94	2.78E-6 3.11E-6 1.48E-6 3.22E-6 2.17E-6 1.74E-6 2.78E-6 3.26E-6 1.03E-6	7.63E-6 1.24E-5 5.15E-6 8.67E-6 4.63E-6 4.25E-6 1.06E-5 1.12E-5 2.43E-6	3.29E-5 3.57E-5 2.82E-5 3.00E-5 9.86E-6 1.12E-5 3.51E-5 > 1.00E-4 5.72E-6	
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.558 0.701 0.520 0.225 0.422 0.465 0.239	1.888 2.147 3.204 1.512 1.913 2.932 2.246	1.926 2.149 3.194 1.396 1.930 2.813 2.112	1.905 2.192 3.084 1.381 2.054 2.926 2.189	1.741 2.370 1.471 0.680 1.580 2.007 1.131	0.233 0.081 0.308 0.126 0.185 0.341 0.286	0.136 0.018 0.035 0.023 0.092 0.139 0.138	103 100 91 101 95 93	101 103 96 90 109 100 97	89 115 35 35 78 63 44	-58 -88 -41 -44 -56 -27 2	-76 -98 -93 -90 -78 -70 -42	1.84E-6 2.09E-6 5.72E-7 5.38E-7 1.61E-6 1.38E-6 7.84E-7	4.02E-6 3.68E-6 2.92E-6 2.79E-6 3.80E-6 5.02E-6 1.13E-5	8.78E-6 6.48E-6 1.50E-5 1.35E-5 8.98E-6 3.44E-5 > 1.00E-4	
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.518 0.944 1.012 0.799 0.973 0.760	1.690 2.879 2.806 2.467 1.917 2.299	1.649 2.725 2.814 2.346 1.752 2.210	1.600 2.692 2.708 2.325 1.641 2.218	1.456 2.781 2.834 2.137 1.712 1.943	0.595 0.640 0.852 1.039 1.539 0.386	0.070 0.036 0.087 0.128 0.153 0.028	96 92 100 93 83 94	92 90 95 91 71 95	80 95 102 80 78 77	7 -32 -16 14 60 -49	-87 -96 -91 -84 -84 -96	2.56E-6 2.26E-6 2.75E-6 2.88E-6 1.17E-5 1.63E-6	1.18E-5 5.58E-6 7.33E-6 1.40E-5 2.60E-5 4.07E-6	4.05E-5 1.89E-5 2.83E-5 4.51E-5 5.78E-5 1.04E-5	
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.293 0.805 0.473 0.492 1.312 0.623 1.114 1.117 0.587	2.074 1.701 1.991 2.342 2.283 1.870 2.920 2.048 2.383	2.082 1.640 1.962 2.316 2.267 1.818 2.873 1.971 2.172	1.998 1.644 1.817 2.271 2.255 1.836 2.844 1.995 2.179	0.216 1.570 1.397 1.492 2.155 1.670 2.626 1.945 1.521	0.014 0.628 0.334 0.495 0.625 0.330 0.036 0.943 0.330	0.016 0.218 0.087 0.099 0.097 0.108 0.018 0.077 0.137	100 93 98 99 98 96 97 92 88	96 94 96 97 97 96 94 89	-26 85 61 54 87 84 84 89 52	-95 -22 -29 -52 -47 -97 -16 -44	-95 -73 -82 -80 -93 -83 -98 -93 -93 -77	2.37E-7 2.14E-6 1.32E-6 1.19E-6 1.84E-6 1.81E-6 1.54E-6 2.36E-6 1.05E-6	6.09E-7 6.24E-6 4.72E-6 1.00E-5 4.20E-6 4.37E-6 2.91E-6 7.09E-6 3.49E-6	2.21E-6 3.55E-5 2.47E-5 9.61E-6 1.21E-5 5.50E-6 2.78E-5 1.54E-5	
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.881 0.472 0.677 0.725 0.604 0.586 0.850	2.472 1.782 1.598 2.142 2.118 2.010 1.586	2.456 1.802 1.569 2.161 2.166 2.017 1.594	2.640 1.798 1.521 2.152 2.090 2.043 1.570	2.522 0.999 1.452 2.210 1.852 1.788 1.759	0.823 0.085 0.872 0.565 0.675 0.612 1.019	0.226 0.007 0.138 0.163 0.027 0.289 0.007	99 102 97 101 103 100 101	111 101 92 101 98 102 98	103 40 84 105 82 84 123	-7 -82 21 -22 5 2 23	-74 -99 -80 -78 -96 -51 -99	3.05E-6 6.92E-7 3.48E-6 2.70E-6 2.61E-6 2.61E-6 5.37E-6	8.71E-6 2.13E-6 1.62E-5 6.69E-6 1.11E-5 1.08E-5 1.54E-5	4.37E-5 5.47E-6 5.08E-5 3.18E-5 3.51E-5 9.67E-5 3.95E-5	
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.788 1.169 0.537 0.594 1.270 0.664 0.886 0.987	2.761 2.042 2.363 2.526 1.904 2.470 1.836 2.663	2.771 2.041 2.440 2.292 1.816 2.360 1.775 2.382	2.641 2.077 2.331 2.350 1.868 2.350 1.833 2.549	2.695 2.235 2.287 2.294 1.913 2.177 1.915 2.535	0.186 1.324 0.236 0.805 0.234 0.677 0.847 0.182	0.007 0.071 0.052 0.040 0.070 0.132 0.001 0.043	100 100 104 88 86 94 94 83	94 104 98 91 94 93 100 93	97 122 96 88 101 84 108 92	-76 18 -56 11 -82 1 -4 -82	-99 -94 -90 -93 -94 -80 -100 -96	1.86E-6 4.91E-6 2.00E-6 3.11E-6 1.91E-6 2.55E-6 3.29E-6 1.75E-6	3.62E-6 1.44E-5 4.27E-6 1.27E-5 3.58E-6 1.02E-5 9.13E-6 3.40E-6	7.03E-6 4.04E-5 9.11E-6 3.84E-5 6.72E-6 4.23E-5 3.00E-5 6.58E-6	
Prostate Cancer PC-3 DU-145	0.736 0.413	1.797 1.518	1.760 1.605	1.835 1.601	1.796 1.444	0.619 0.659	0.123 -0.003	97 108	104 108	100 93	-16 22	-83 -100	2.70E-6 4.07E-6	7.29E-6 1.52E-5	3.20E-5 3.90E-5	
Breast Cancer MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.396 0.568 0.973 1.343 0.680 0.703	1.952 1.409 1.916 2.703 1.288 1.372	1.864 1.450 1.854 2.705 1.220 1.336	1.802 1.455 1.849 2.624 1.204 1.335	0.710 1.385 1.906 2.523 1.158 1.253	0.333 0.548 1.260 1.020 0.726 0.279	0.139 0.137 0.778 0.007 0.258 0.127	94 105 93 100 89 95	90 106 93 94 86 94	20 97 99 87 79 82	-16 -4 30 -24 7 -60	-65 -76 -20 -99 -62 -82	3.76E-7 2.94E-6 5.18E-6 2.15E-6 2.52E-6 1.68E-6	3.62E-6 9.23E-6 4.01E-5 6.07E-6 1.28E-5 3.77E-6	4.96E-5 4.39E-5 > 1.00E-4 2.21E-5 6.71E-5 8.46E-6	

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results																
NSC : D - 782	788 / 1				Exp	Experiment ID : 1501NS15							Туре : 08	Units : N	Units : Molar	
Report Date :	Decem	ber 27, 2	2015		Tes	Test Date : January 12, 2015						QNS	:	MC :		
COMI : KCN-F	-GJ-30				Sta	in Rea	gent : S	RB Dual	Pass F	Related	I	SSPL	: 0ZAS			
	_					Lo	og10 Co	ncentration								
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	-6.0	-5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	-5.0	-4.0	GI50	TGI	LC50	
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.717 0.653 0.199 0.703 1.023 0.437	2.224 1.845 1.304 2.348 2.377 1.718	2.419 1.775 1.330 2.340 2.500 1.614	2.326 1.616 1.196 2.181 2.655 1.641	0.964 1.216 0.445 1.632 0.989 1.049	0.544 0.589 0.244 0.606 0.791 0.348	0.458 0.432 0.182 0.607 0.638 0.370	113 94 102 99 109 92	107 81 90 90 120 94	16 47 22 56 -3 48	-24 -10 -14 -23 -20	-36 -34 -9 -14 -38 -15	4.25E-7 8.24E-7 3.91E-7 1.24E-6 3.71E-7 8.96E-7	2.53E-6 6.71E-6 2.07E-5 6.36E-6 9.39E-7 5.01E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4	
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.479 0.760 0.811 1.204 1.302 0.666 0.626 0.184 1.034	1.581 2.286 2.226 1.534 2.343 1.975 1.854 1.997 2.215	1.450 2.106 2.080 1.486 2.313 1.871 1.731 2.089 2.127	1.573 2.167 2.200 1.461 2.318 1.932 1.693 2.019 2.042	1.608 2.135 2.224 1.542 2.396 1.708 1.564 1.639 1.784	0.332 0.867 0.581 0.646 0.926 0.368 0.339 0.085 0.259	0.089 -0.007 0.065 0.003 0.095 0.126 0.116 0.036 0.063	88 90 86 97 92 90 105 93	99 92 98 78 98 97 87 101 85	102 90 100 103 105 80 76 80 64	-31 7 -28 -46 -29 -45 -46 -54 -54	-82 -100 -92 -100 -93 -81 -82 -81 -94	2.48E-6 3.04E-6 2.45E-6 2.55E-6 1.73E-6 1.64E-6 1.68E-6 1.25E-6	5.88E-6 1.16E-5 6.01E-6 4.88E-6 6.08E-6 4.37E-6 4.21E-6 3.97E-6 2.88E-6	2.40E-5 3.41E-5 2.19E-5 2.14E-5 1.39E-5 1.31E-5 9.37E-6 6.60E-6	
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.622 1.230 0.356 0.304 0.284 0.491 0.296	2.030 3.361 2.334 2.044 1.576 2.883 2.220	1.900 3.365 2.257 1.907 1.575 2.867 2.240	2.028 3.319 2.272 1.953 1.681 2.791 2.346	1.859 3.427 0.273 1.013 1.413 2.133 0.910	0.239 0.103 0.036 0.147 0.043 0.138 0.132	0.217 0.089 0.026 0.030 0.084 0.109 0.095	91 100 96 92 100 99 101	100 98 97 95 108 96 107	88 103 -23 41 87 69 32	-62 -92 -90 -52 -85 -72 -55	-65 -93 -93 -90 -70 -78 -68	1.79E-6 1.87E-6 2.45E-7 6.74E-7 1.65E-6 1.36E-6 5.72E-7	3.87E-6 3.38E-6 6.40E-7 2.75E-6 3.21E-6 3.08E-6 2.32E-6	8.37E-6 6.11E-6 9.56E-6 6.26E-6 6.29E-6 8.67E-6	
CNS Cancer SF-268 SF-295 SNB-19 SNB-75 U251	0.582 1.038 1.209 0.966 0.375	2.229 3.338 2.863 1.951 1.526	2.179 3.182 2.783 1.703 1.464	2.044 3.344 2.826 1.693 1.455	1.900 3.353 2.732 1.627 0.714	0.466 0.949 1.391 1.379 0.026	0.050 -0.002 0.109 0.001	97 93 95 75 95	89 100 98 74 94	80 101 92 67 29	-20 -9 11 42 -93	-91 -100 -91 -100 -100	2.00E-6 2.91E-6 3.30E-6 4.78E-6 4.80E-7	6.31E-6 8.34E-6 1.28E-5 1.97E-5 1.74E-6	2.63E-5 2.84E-5 3.96E-5 4.44E-5 4.44E-6	
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.205 0.783 0.484 0.515 1.113 0.575 0.773 0.918 0.535	1.501 1.784 1.852 2.679 1.909 1.952 2.797 1.558 2.019	1.449 1.779 1.744 2.539 1.865 1.844 2.760 1.543 1.940	1.316 1.697 1.765 2.605 1.838 1.879 2.711 1.584 1.952	0.094 1.581 1.100 1.275 1.838 1.568 1.991 1.503 1.561	0.025 0.320 0.268 0.278 0.632 0.134 0.073 0.622 0.165	0.062 0.120 0.055 0.019 0.115 0.090 -0.007 0.042 0.091	96 99 92 94 95 92 98 98 98	86 91 97 91 95 96 104 95	-54 80 45 35 91 72 60 91 69	-88 -59 -45 -46 -43 -77 -91 -32 -69	-70 -85 -96 -90 -84 -100 -95 -83	1.80E-7 1.64E-6 7.90E-7 2.02E-6 1.41E-6 1.17E-6 2.16E-6 1.38E-6	4.10E-7 3.75E-6 3.17E-6 2.70E-6 4.77E-6 3.05E-6 2.51E-6 5.49E-6 3.16E-6	9.34E-7 8.59E-6 1.32E-5 1.19E-5 1.40E-5 6.61E-6 5.38E-6 1.91E-5 7.27E-6	
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.704 0.402 0.615 0.803 0.565 0.709 1.189	2.427 1.446 1.467 2.134 1.815 2.295 2.310	2.372 1.421 1.359 2.053 1.894 2.247 2.219	2.329 1.418 1.386 2.100 1.918 2.234 2.330	2.225 0.696 1.275 2.211 1.776 2.147 2.370	0.627 0.032 0.771 0.734 0.520 0.839 1.484	0.184 0.003 0.019 0.155 0.088 0.521 -0.015	97 98 87 94 106 97 92	94 97 91 97 108 96 102	88 28 78 106 97 91 105	-11 -92 18 -9 -8 8 26	-74 -99 -97 -81 -84 -27 -100	2.43E-6 4.83E-7 2.92E-6 3.07E-6 2.80E-6 3.11E-6 5.01E-6	7.75E-6 1.71E-6 1.44E-5 8.41E-6 8.38E-6 1.72E-5 1.61E-5	4.17E-5 4.46E-6 3.91E-5 3.75E-5 3.54E-5 > 1.00E-4 4.02E-5	
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.746 1.555 0.519 0.577 0.951 0.597 0.974 0.674	2.386 2.459 2.263 3.008 1.576 2.074 1.778 2.539	2.234 2.391 2.133 2.874 1.581 2.108 1.728 2.463	2.286 2.412 2.214 2.895 1.590 2.088 1.664 2.427	2.350 2.505 2.176 2.583 1.552 2.014 1.902 2.380	0.198 1.393 0.160 0.604 0.088 0.457 0.938 0.236	-0.012 0.014 0.055 -0.010 0.107 0.188 -0.015 0.125	91 92 93 94 101 102 94 96	94 95 97 102 101 86 94	98 105 95 83 96 96 115 91	-73 -10 -69 1 -91 -24 -4 -65	-100 -99 -89 -100 -89 -69 -100 -82	1.90E-6 3.00E-6 1.88E-6 2.51E-6 1.76E-6 2.42E-6 3.54E-6 1.84E-6	3.72E-6 8.12E-6 3.79E-6 1.03E-5 3.27E-6 6.35E-6 9.31E-6 3.84E-6	7.30E-6 2.79E-5 7.64E-6 3.20E-5 6.05E-6 3.87E-5 3.03E-5 8.02E-6	
Prostate Cancer PC-3 DU-145	0.505 0.451	1.773 2.182	1.812 2.214	1.804 2.112	1.509 2.000	0.168 0.591	0.002 -0.017	103 102	102 96	79 89	-67 8	-100 -100	1.58E-6 3.05E-6	3.49E-6 1.19E-5	7.68E-6 3.45E-5	
Breast Cancer MCF7 MDA-MB-231/ATC HS 578T BT-549 T-47D MDA-MB-468	0.509 C 0.736 1.280 1.037 0.727 0.815	2.670 1.838 2.347 2.232 1.564 1.297	2.378 1.860 2.347 2.092 1.433 1.265	2.389 1.868 2.350 2.155 1.473 1.258	0.988 1.851 2.327 1.767 1.226 1.127	0.297 0.729 1.611 0.510 0.648 0.259	0.282 0.172 1.031 0.001 0.455 0.288	87 102 100 88 84 93	87 103 100 94 89 92	22 101 98 61 60 65	-42 -1 31 -51 -11 -68	-45 -77 -19 -100 -37 -65	3.72E-7 3.17E-6 5.21E-6 1.25E-6 1.37E-6 1.29E-6	2.22E-6 9.77E-6 4.12E-5 3.51E-6 7.00E-6 3.06E-6	 > 1.00E-4 4.44E-5 > 1.00E-4 9.83E-6 > 1.00E-4 7.29E-6 	

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results																
NSC : D - 786	6062 / 1				Exp	Experiment ID : 1509NS56							Гуре : 08	Units : N	Iolar	
Report Date :	Decemb	ber 27, 2	2015		Tes	Test Date : September 08, 2015						QNS	:	MC :		
COMI : KCN-I	PGJ-60				Sta	in Rea	gent : S	RB Dual	Pass F	Related	I	SSPL	: 0ZAS			
	-				0.1	Lo	og10 Cor	ncentration								
Panel/Cell Line	Time Zero	Ctrl	-8.5	Mear -7.5	-6.5	-5.5	es -4.5	-8.5	Р -7.5	ercent G -6.5	-5.5	-4.5	GI50	TGI	LC50	
Ceukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.854 0.734 0.259 0.951 0.482 0.285	3.339 3.171 2.584 3.315 1.727 0.873	3.368 3.124 2.577 3.295 1.686 0.899	3.346 3.086 2.541 3.317 1.722 0.850	3.013 2.913 2.328 3.064 1.369 0.722	0.943 0.666 0.255 0.868 0.327 0.297	0.738 0.588 0.149 0.721 0.291 0.218	101 98 100 99 97 104	100 97 98 100 100 96	87 89 89 71 74	4 -9 -2 -9 -32 2	-14 -20 -43 -24 -40 -24	9.23E-7 8.35E-7 8.98E-7 8.39E-7 5.34E-7 7.20E-7	5.36E-6 2.68E-6 3.20E-6 2.71E-6 1.62E-6 3.97E-6	> 3.33E-5 > 3.33E-5 > 3.33E-5 > 3.33E-5 > 3.33E-5 > 3.33E-5 > 3.33E-5	
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.397 0.829 0.551 1.496 0.568 0.617 0.662 0.217 0.922	2.097 2.115 1.674 1.999 1.530 1.773 1.870 2.547 2.553	2.036 2.043 1.654 1.916 1.445 1.693 1.766 2.577 2.514	1.977 1.986 1.589 1.863 1.452 1.691 1.767 2.556 2.452	2.019 2.017 1.626 1.872 1.480 1.697 1.767 2.536 2.321	1.532 0.623 0.563 1.904 0.363 0.343 1.384 0.331 0.783	0.406 0.039 0.306 0.511 0.194 0.140 0.475 0.075 0.285	96 94 83 91 93 91 101 98	93 90 92 73 92 93 92 100 94	95 92 96 75 95 93 91 100 86	67 -25 -36 -44 60 5 -15	1 -95 -44 -66 -66 -77 -28 -65 -69	5.96E-6 7.66E-7 1.01E-6 5.43E-6 7.32E-7 6.87E-7 4.30E-6 1.11E-6 7.53E-7	> 3.33E-5 2.04E-6 3.51E-6 1.19E-5 1.76E-6 1.58E-6 1.59E-5 3.91E-6 2.36E-6	> 3.33E-5 7.58E-6 > 3.33E-5 2.60E-5 9.73E-6 4.90E-6 > 3.33E-5 2.01E-5 1.47E-5	
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.482 0.664 0.329 0.237 0.374 0.429 0.230	1.542 2.151 2.863 1.485 2.259 2.524 1.947	1.583 2.085 2.826 1.388 2.242 2.397 1.901	1.540 2.089 3.099 1.330 2.269 2.374 1.893	1.621 2.257 2.695 1.315 2.357 2.406 1.893	0.532 0.774 0.221 0.095 0.346 0.367 0.334	0.137 0.102 0.033 0.049 0.116 0.042 0.081	104 96 99 92 99 94 97	100 96 109 88 101 93 97	107 107 93 86 105 94 97	5 7 -33 -60 -8 -14 6	-72 -85 -90 -79 -69 -90 -65	1.21E-6 1.24E-6 7.34E-7 5.90E-7 1.03E-6 8.52E-7 1.09E-6	3.83E-6 4.01E-6 1.83E-6 1.29E-6 2.85E-6 2.45E-6 4.05E-6	1.73E-5 1.40E-5 6.61E-6 2.84E-6 1.63E-5 9.81E-6 2.05E-5	
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.431 0.834 0.954 0.499 0.861 0.301	1.734 2.617 2.543 1.756 1.613 1.529	1.662 2.505 2.543 1.759 1.500 1.511	1.608 2.497 2.502 1.791 1.465 1.459	1.554 2.559 2.436 1.744 1.504 1.267	0.507 1.203 1.025 0.663 1.167 0.181	0.127 0.443 0.095 0.095 0.078 0.033	95 94 100 100 85 98	90 93 97 103 80 94	86 97 93 99 86 79	6 21 4 13 41 -40	-71 -47 -90 -81 -91 -89	9.39E-7 1.37E-6 1.02E-6 1.24E-6 2.07E-6 5.81E-7	3.97E-6 6.74E-6 3.71E-6 4.58E-6 6.79E-6 1.53E-6	1.79E-5 > 3.33E-5 1.25E-5 1.56E-5 1.63E-5 5.35E-6	
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-62	0.426 0.729 0.602 0.472 0.964 0.780 0.839 0.703	2.654 1.351 2.750 2.446 1.799 2.177 2.836 2.427	2.512 1.273 2.678 2.396 1.824 2.176 2.775 2.300	2.457 1.293 2.635 2.350 1.804 2.175 2.699 2.289	2.326 1.289 2.559 2.262 1.805 2.120 2.727 2.062	0.063 0.622 0.777 0.316 1.146 0.638 0.183 0.336	0.054 0.097 0.217 0.111 0.268 0.097 0.027 0.165	94 88 97 103 100 97 93	91 95 95 101 100 93 92	85 90 91 91 101 96 95 79	-85 -15 8 -33 22 -18 -78 -52	-87 -64 -76 -72 -88 -97 -77	5.36E-7 8.03E-7 1.04E-6 7.10E-7 1.46E-6 8.40E-7 6.03E-7 5.53E-7	1.05E-6 2.41E-6 4.32E-6 1.80E-6 5.67E-6 2.31E-6 1.17E-6 1.33E-6	2.07E-6 1.03E-5 2.13E-5 8.18E-6 1.93E-5 9.57E-6 2.29E-6 3.20E-6	
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.829 0.442 0.661 0.754 0.496 0.560 0.802	2.170 1.541 1.487 2.088 2.110 1.793 1.460	2.136 1.520 1.457 2.010 2.083 1.772 1.421	2.053 1.495 1.377 2.012 2.030 1.692 1.402	1.920 1.473 1.340 2.007 1.893 1.723 1.442	0.756 0.220 0.697 1.181 0.617 0.529 1.269	0.266 0.012 0.043 0.409 0.276 0.318 0.669	98 96 94 98 98 98	91 96 87 94 95 92 91	81 94 82 94 87 94 97	-9 -50 4 32 7 -6 71	-68 -97 -93 -46 -44 -43 -17	7.42E-7 6.71E-7 8.62E-7 1.70E-6 9.66E-7 9.25E-7 5.78E-6	2.66E-6 1.49E-6 3.68E-6 8.58E-6 4.64E-6 2.93E-6 2.15E-5	1.66E-5 3.32E-6 1.20E-5 > 3.33E-5 > 3.33E-5 > 3.33E-5 > 3.33E-5	
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.605 1.169 0.483 0.592 0.963 0.648 0.762 0.811	2.530 2.057 1.992 2.133 1.682 2.113 1.610 2.129	2.455 2.000 1.979 1.930 1.619 2.051 1.557 1.882	2.373 2.010 1.958 1.948 1.613 2.088 1.536 1.956	2.370 2.076 1.902 1.889 1.566 2.060 1.615 1.966	0.732 2.261 0.729 0.848 0.947 0.526 1.056 1.015	0.133 0.256 0.094 0.259 0.152 0.207 0.462 0.086	96 94 99 87 91 96 94 81	92 95 98 88 90 98 91 87	92 102 94 84 84 96 101 88	7 123 16 17 -2 -19 35 15	-78 -81 -56 -84 -68 -39 -89	1.03E-6 7.68E-6 1.23E-6 1.07E-6 8.27E-7 8.41E-7 1.95E-6 1.10E-6	3.98E-6 1.36E-5 4.90E-6 5.62E-6 3.18E-6 2.29E-6 9.78E-6 4.67E-6	1.55E-5 2.41E-5 1.61E-5 2.73E-5 1.43E-5 1.43E-5 > 3.33E-5 1.40E-5	
Prostate Cancer PC-3 DU-145	0.649 0.284	2.629 1.464	2.527 1.488	2.459 1.416	2.403 1.439	0.598 0.510	0.180 0.096	95 102	91 96	89 98	-8 19	-72 -66	8.36E-7 1.35E-6	2.76E-6 5.57E-6	1.50E-5 2.14E-5	
Breast Cancer MCF7 MDA-MB-231/ATC HS 578T BT-549 T-47D MDA-MB-468	0.405 C 0.619 1.054 1.183 0.750 0.794	2.289 1.723 2.117 2.295 1.609 1.691	2.145 1.694 2.069 2.246 1.535 1.614	2.076 1.729 2.029 2.249 1.534 1.553	1.785 1.681 1.996 2.254 1.440 1.532	0.550 0.549 1.126 0.769 0.753 0.833	0.082 0.267 0.854 0.235 0.593 0.180	92 97 95 96 91 91	89 101 92 96 91 85	73 96 89 96 80 82	8 -11 7 -35 4	-80 -57 -19 -80 -21 -77	7.54E-7 8.95E-7 9.86E-7 7.50E-7 7.96E-7 8.64E-7	4.08E-6 2.61E-6 6.10E-6 1.80E-6 3.44E-6 3.76E-6	1.52E-5 2.35E-5 > 3.33E-5 7.16E-6 > 3.33E-5 1.54E-5	

Developmental Ther	apeutics Program	NSC: D-786063 / 1	Conc: 1.00E-5 Molar	Test Date: Aug 10, 2015				
One Dose Mea	an Graph	Experiment ID: 1508	Experiment ID: 1508OS37					
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Per	cent				
Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer	112.64 100.37 104.74 99.66 98.95 102.98		-					
A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H23 NCI-H322M NCI-H460 NCI-H522	101.89 95.31 88.81 65.62 102.73 94.10 101.07 104.61 91.97							
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer	106.42 105.57 73.88 95.62 115.28 99.36 123.42							
SF-268 SF-295 SF-539 SNB-19 SNB-75 U251 Melanoma	95.42 99.80 100.47 114.13 83.54 110.78		-					
MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-62	90.61 90.61 93.97 98.67 103.11 101.96 95.01 102.43							
OVarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3 Based Conser	106.04 108.80 104.55 98.49 99.81 104.04 84.06							
Refail California 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31 Prostate Cancer	93.26 104.47 100.67 84.48 107.84 99.62 92.20 99.48							
PC-3 DU-145 Breast Cancer MCF7 MDA-MB-231/ATCC HS 578T BT-549 T-47D	88.80 101.10 76.68 108.82 105.05 88.36 84.72							
MDA-MB-468 Mean Delta Range	105.82 98.61 32.99 57.80							
	L 150	100 50	0 -50	-100 -150				

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results																
NSC : D - 782	789 / 1				Experiment ID : 1501NS15							Test	Test Type : 08		Units : Molar	
Report Date :	Decemb	oer 27, 2	2015		Tes	Test Date : January 12, 2015							:	MC :		
COMI : KCN-F	PGJ-31				Sta	in Rea	gent : S	RB Dual	Pass	Related	ł	SSP	L:0ZAS			
						L	og10 Cor	ncentration	_							
Panel/Cell Line	Time Zero	Ctrl	-8.0	Mear -7.0	Optica -6.0	I Densiti -5.0	es -4.0	-8.0	F -7.0	ercent G -6.0	Fowth -5.0	-4.0	GI50	TGI	LC50	
Leukemia CCRF-CEM RPMI-8226	0.717 1.023	2.116 2.332	2.145 2.508	2.225 2.419	1.545 1.736	0.674 0.806	0.402 0.580	102 113	108 107	59 54	-6 -21	-44 -43	1.38E-6 1.14E-6	8.07E-6 5.24E-6	> 1.00E-4 > 1.00E-4	
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	Cancer 0.479 0.760 0.811 1.204 1.302 0.666 0.626 0.184 1.034	1.496 2.250 2.002 1.575 2.332 1.924 1.757 1.949 2.101	1.541 2.165 1.921 1.508 2.294 1.895 1.706 2.027 1.882	1.538 2.090 1.951 1.547 2.198 1.872 1.729 1.958 1.962	1.512 2.166 2.091 1.669 2.331 1.820 1.551 1.710 1.761	0.341 1.121 0.704 0.891 0.842 0.431 0.689 0.155 0.086	0.131 -0.012 0.058 0.040 0.073 0.153 0.047 0.061 0.057	104 94 93 82 96 98 95 104 79	104 89 96 92 87 96 98 100 87	102 94 107 126 100 92 82 86 68	-29 24 -13 -26 -35 -35 6 -16 -92	-73 -100 -93 -97 -94 -77 -92 -67 -95	2.49E-6 4.29E-6 2.99E-6 2.34E-6 2.34E-6 2.13E-6 2.61E-6 2.27E-6 1.30E-6	6.01E-6 1.57E-5 7.77E-6 6.74E-6 5.48E-6 5.28E-6 1.14E-5 6.97E-6 2.67E-6	3.04E-5 3.96E-5 2.89E-5 2.19E-5 1.77E-5 2.25E-5 3.69E-5 4.62E-5 5.48E-6	
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.622 1.230 0.356 0.304 0.284 0.491 0.296	1.956 3.308 2.486 2.148 1.495 2.865 2.210	1.946 3.268 2.344 2.025 1.539 2.852 2.087	1.875 3.370 2.342 1.956 1.647 2.789 2.170	1.906 3.404 1.440 1.658 1.460 2.348 1.612	0.332 0.254 0.076 0.232 0.075 0.260 0.220	0.158 0.090 -0.007 -0.006 0.057 0.083 0.118	99 98 93 93 104 99 94	94 103 93 90 113 97 98	96 105 51 73 97 78 69	-47 -79 -79 -24 -74 -47 -26	-75 -93 -100 -100 -80 -83 -60	2.11E-6 1.98E-6 1.02E-6 1.74E-6 1.89E-6 1.68E-6 1.58E-6	4.72E-6 3.70E-6 2.47E-6 5.69E-6 3.70E-6 4.21E-6 5.33E-6	1.32E-5 6.93E-6 6.01E-6 2.21E-5 7.26E-6 1.20E-5 5.06E-5	
CNS Cancer SF-268 SF-295 SNB-19 SNB-75 U251	0.582 1.038 1.209 0.966 0.375	2.210 3.307 2.894 1.958 1.510	2.189 3.216 2.759 1.806 1.480	2.178 3.197 2.749 1.747 1.509	2.039 3.333 2.740 1.777 1.170	0.675 0.766 1.949 1.496 0.211	0.123 0.024 0.150 -0.016 0.001	99 96 92 85 97	98 95 91 79 100	90 101 91 82 70	6 -26 44 53 -44	-79 -98 -88 -100 -100	2.96E-6 2.52E-6 7.43E-6 1.05E-5 1.50E-6	1.17E-5 6.23E-6 2.16E-5 2.23E-5 4.12E-6	4.55E-5 2.15E-5 5.18E-5 4.72E-5 1.29E-5	
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.205 0.783 0.484 0.515 1.113 0.575 0.773 0.918 0.535	1.496 1.752 1.855 2.758 1.849 1.922 2.659 1.523 1.926	1.405 1.710 1.834 2.703 1.796 1.920 2.589 1.507 1.803	1.278 1.722 1.751 2.571 1.847 1.918 2.616 1.519 1.873	0.494 1.642 1.696 2.184 1.823 1.811 2.363 1.427 1.468	0.050 0.512 0.402 0.366 0.765 0.265 0.045 0.624 0.212	-0.001 0.176 0.066 0.018 0.081 0.056 -0.013 0.068 0.094	93 96 98 93 100 96 97 91	83 97 92 92 100 100 98 99 96	22 89 88 74 96 92 84 84 67	-76 -35 -17 -29 -31 -54 -94 -32 -60	-100 -78 -97 -93 -90 -100 -93 -83	3.50E-7 2.06E-6 2.31E-6 1.72E-6 1.93E-6 1.56E-6 1.56E-6 1.97E-6 1.36E-6	1.69E-6 5.23E-6 6.89E-6 5.69E-6 4.26E-6 2.97E-6 5.30E-6 3.36E-6	5.48E-6 2.28E-5 2.05E-5 2.02E-5 9.39E-6 5.66E-6 1.98E-5 8.29E-6	
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.704 0.402 0.615 0.803 0.565 0.709 1.189	2.435 1.447 1.457 2.110 1.740 2.268 2.260	2.454 1.433 1.460 2.086 1.772 2.300 2.277	2.433 1.472 1.374 2.040 1.813 2.217 2.226	2.302 1.024 1.299 2.286 1.634 2.072 2.331	0.809 0.259 0.810 0.881 0.634 0.772 1.317	0.243 -0.018 0.127 0.186 0.033 0.415 -0.014	101 99 100 98 103 102 102	100 102 90 95 106 97 97	92 60 81 113 91 87 107	6 -36 23 6 6 4 12	-66 -100 -79 -77 -94 -42 -100	3.09E-6 1.26E-6 3.45E-6 3.89E-6 3.03E-6 2.81E-6 3.96E-6	1.22E-5 4.23E-6 1.68E-5 1.18E-5 1.14E-5 1.23E-5 1.28E-5	6.06E-5 1.67E-5 5.17E-5 3.62E-5 3.62E-5 > 1.00E-4 3.57E-5	
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.746 1.555 0.519 0.577 0.951 0.597 0.974 0.674	2.381 2.332 2.293 3.050 1.637 2.060 1.784 2.475	2.316 2.176 2.228 3.041 1.624 1.969 1.725 2.376	2.286 2.146 2.235 2.930 1.634 1.997 1.761 2.414	2.430 2.409 2.025 2.482 1.648 1.935 1.970 2.167	0.140 1.253 0.120 0.273 0.213 0.468 0.749 0.186	-0.011 0.035 -0.029 0.082 0.128 -0.036 0.058	96 80 96 100 98 94 93 94	94 76 97 95 100 96 97 97	103 110 85 77 102 91 123 83	-81 -19 -77 -53 -78 -22 -23 -72	-100 -100 -93 -100 -91 -79 -100 -91	1.94E-6 2.90E-6 1.64E-6 1.62E-6 1.94E-6 2.32E-6 3.16E-6 1.63E-6	3.62E-6 7.07E-6 3.35E-6 3.69E-6 6.43E-6 6.95E-6 3.42E-6	6.77E-6 2.39E-5 6.82E-6 9.52E-6 7.01E-6 3.15E-5 2.24E-5 7.17E-6	
Prostate Cancer PC-3 DU-145	0.505 0.451	1.795 2.147	1.826 2.180	1.808 2.155	1.690 1.812	0.333 0.524	0.086 -0.031	102 102	101 100	92 80	-34 4	-83 -100	2.15E-6 2.50E-6	5.36E-6 1.10E-5	2.11E-5 3.32E-5	
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.509 0.736 1.280 1.037 0.727 0.815	2.787 1.872 2.311 2.240 1.440 1.325	2.568 1.858 2.208 2.236 1.437 1.269	2.439 1.897 2.184 2.148 1.392 1.317	1.447 1.946 2.307 2.137 1.315 1.100	0.632 0.916 1.600 0.710 0.850 0.272	0.143 0.209 0.900 -0.010 0.175 0.163	90 99 90 100 100 89	85 102 88 92 93 98	41 106 100 91 82 56	5 16 31 -32 17 -67	-72 -72 -30 -100 -76 -80	6.26E-7 4.20E-6 5.29E-6 2.17E-6 3.14E-6 1.12E-6	1.17E-5 1.52E-5 3.24E-5 5.54E-6 1.53E-5 2.86E-6	5.21E-5 5.66E-5 > 1.00E-4 1.86E-5 5.26E-5 7.31E-6	
		Natio	onal	Cano	er Ir	nstitu In-	ite Do Vitro	evelop Testir	mer ng R	ital T esult	hera s	peuti	cs Program	1		
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NSC : D - 782	786 / 1				Exp	erimer	nt ID:1	501NS15	5			Test	Туре : 08	Units : N	lolar	
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Janua	ary 12, 20	15			QNS	:	MC :		
COMI : KCN-F	PGJ-28				Sta	in Rea	gent : S	RB Dual	Pass I	Related	ł	SSPI	_ : 0ZAS			
	Time			Maar	Onting	Lo	og10 Cor	ncentration		oreant C						
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	es -4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50	
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.717 0.653 0.199 0.703 1.023 0.437	2.211 1.866 1.284 2.361 2.381 1.645	2.300 1.678 1.282 2.351 2.469 1.594	2.253 1.554 1.269 2.376 2.460 1.506	1.632 1.483 0.879 2.034 1.688 1.107	0.674 0.580 0.286 0.713 0.880 0.422	0.391 0.554 0.236 0.630 0.598 0.382	106 85 100 99 106 96	103 74 99 101 106 88	61 68 63 80 49 55	-6 -11 8 1 -14 -3	-45 -15 -10 -42 -13	1.47E-6 1.70E-6 1.70E-6 2.40E-6 9.57E-7 1.24E-6	8.13E-6 7.24E-6 > 1.00E-4 1.13E-5 5.99E-6 8.74E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4	
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	Cancer 0.479 0.760 0.811 1.204 1.302 0.666 0.626 0.184 1.034	1.546 2.292 1.923 1.491 2.373 1.972 1.785 1.874 2.047	1.506 2.092 1.775 1.489 2.301 1.874 1.724 1.984 1.999	1.554 2.157 1.910 1.487 2.371 1.814 1.659 1.887 1.960	1.521 2.105 1.918 1.591 2.332 1.781 1.531 1.473 1.786	0.386 1.088 0.508 0.857 0.752 0.326 0.672 0.098 0.470	0.156 0.033 0.094 0.055 0.087 0.213 0.111 0.053 0.316	96 87 99 93 92 95 106 95	101 99 99 100 88 89 101 91	98 88 100 135 96 85 78 76 74	-20 21 -37 -29 -42 -51 4 -47 -55	-68 -96 -95 -93 -68 -82 -71 -69	2.55E-6 3.71E-6 2.30E-6 3.30E-6 2.15E-6 1.82E-6 1.82E-6 1.63E-6 1.63E-6 1.54E-6	6.81E-6 1.52E-5 5.33E-6 6.66E-6 4.95E-6 4.22E-6 1.11E-5 4.15E-6 3.77E-6	4.31E-5 4.07E-5 1.76E-5 2.08E-5 1.42E-5 9.81E-6 4.22E-5 1.33E-5 9.21E-6	
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.622 1.230 0.356 0.304 0.284 0.491 0.296	1.887 3.381 2.342 2.154 1.594 2.655 2.275	1.738 3.401 2.236 1.963 1.606 2.633 2.241	1.865 3.376 2.267 1.995 1.639 2.586 2.304	1.662 3.358 1.100 1.549 1.299 2.033 1.479	0.274 0.128 0.059 0.219 0.074 0.055 0.207	0.139 0.227 0.020 0.051 0.095 0.012 0.071	88 101 95 90 101 99 98	98 100 96 91 103 97 101	82 99 37 67 77 71 60	-56 -90 -83 -28 -74 -89 -30	-78 -82 -94 -83 -67 -98 -76	1.71E-6 1.82E-6 6.12E-7 1.52E-6 1.52E-6 1.36E-6 1.28E-6	3.93E-6 3.35E-6 2.04E-6 5.09E-6 3.25E-6 2.79E-6 4.63E-6	9.04E-6 6.16E-6 5.29E-6 2.51E-5 6.95E-6 5.72E-6 2.71E-5	
CNS Cancer SF-268 SF-295 SNB-19 SNB-75 U251	0.582 1.038 1.209 0.966 0.375	2.138 3.317 2.864 1.868 1.499	2.084 3.151 2.789 1.660 1.530	2.049 3.236 2.844 1.661 1.478	1.933 3.290 2.803 1.613 1.062	0.709 0.756 1.890 1.462 0.240	0.202 0.089 0.154 0.004 0.024	97 93 95 77 103	94 96 99 77 98	87 99 96 72 61	8 -27 41 55 -36	-65 -91 -87 -100 -94	2.94E-6 2.44E-6 6.91E-6 1.08E-5 1.30E-6	1.29E-5 6.08E-6 2.09E-5 2.27E-5 4.26E-6	6.19E-5 2.26E-5 5.13E-5 4.78E-5 1.75E-5	
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.205 0.783 0.484 0.515 1.113 0.575 0.773 0.918 0.535	1.485 1.783 1.799 2.740 1.945 1.989 2.663 1.482 1.987	1.372 1.742 1.723 2.633 1.927 1.895 2.683 1.442 1.997	1.311 1.709 1.713 2.639 1.892 1.913 2.671 1.475 2.011	0.382 1.663 1.515 2.084 1.851 1.771 2.475 1.419 1.508	0.051 0.440 0.303 0.437 0.871 0.188 -0.010 0.611 0.235	0.019 0.205 0.073 0.048 0.185 0.114 -0.012 0.097 0.130	91 96 94 95 98 93 101 93 101	86 93 95 94 95 100 99 102	14 88 70 89 85 90 89 67	-75 -44 -37 -15 -22 -67 -100 -33 -56	-91 -74 -85 -91 -83 -80 -100 -89 -76	3.17E-7 1.94E-6 1.76E-6 2.24E-6 1.69E-6 1.62E-6 2.08E-6 1.37E-6	1.43E-6 4.65E-6 6.64E-6 6.35E-6 3.60E-6 2.98E-6 5.32E-6 3.50E-6	5.22E-6 1.60E-5 1.84E-5 2.89E-5 2.87E-5 7.69E-6 5.46E-6 1.98E-5 8.91E-6	
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.704 0.402 0.615 0.803 0.565 0.709 1.189	2.419 1.362 1.476 2.135 1.751 2.268 2.184	2.472 1.376 1.356 1.944 1.818 2.204 2.095	2.417 1.370 1.348 2.042 1.814 2.184 2.202	2.285 0.953 1.232 2.074 1.517 1.991 2.177	0.736 0.257 0.846 0.355 0.574 0.728 1.103	0.253 0.007 0.212 0.076 0.066 0.322 0.029	103 101 86 86 106 96 91	100 101 85 93 105 95 102	92 57 72 95 80 82 99	2 -36 27 -56 1 -7	-64 -98 -66 -91 -88 -55 -98	2.93E-6 1.20E-6 2.00E-6 2.40E-6 2.40E-6 2.50E-6 2.90E-6	1.07E-5 4.11E-6 1.95E-5 4.28E-6 1.02E-5 1.05E-5 8.54E-6	6.12E-5 1.67E-5 6.79E-5 9.16E-6 3.71E-5 8.28E-5 2.97E-5	
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.746 1.555 0.519 0.577 0.951 0.597 0.974 0.674	2.402 2.398 2.247 3.113 1.647 2.187 1.795 2.567	2.217 2.346 2.151 2.893 1.606 2.241 1.720 2.367	2.399 2.404 2.235 2.990 1.659 2.207 1.766 2.389	2.288 2.436 1.912 2.223 1.576 1.914 1.909 2.124	0.192 0.890 0.112 0.339 0.101 0.560 0.718 0.207	0.022 0.008 0.065 -0.008 0.051 0.174 0.024 0.122	89 94 91 94 103 91 89	100 101 99 95 102 101 96 91	93 104 81 65 90 83 114 77	-74 -43 -78 -41 -89 -6 -26 -69	-97 -99 -88 -100 -95 -71 -98 -82	1.81E-6 2.34E-6 1.56E-6 1.38E-6 1.67E-6 2.33E-6 2.86E-6 1.52E-6	3.60E-6 5.12E-6 3.21E-6 4.08E-6 3.17E-6 8.50E-6 6.49E-6 3.35E-6	7.16E-6 1.34E-5 6.63E-6 1.41E-5 6.03E-6 4.74E-5 2.15E-5 7.38E-6	
Prostate Cancer PC-3 DU-145	0.505 0.451	1.764 2.088	1.755 2.132	1.796 2.060	1.603 1.758	0.298 0.637	0.090 0.003	99 103	103 98	87 80	-41 11	-82 -99	1.95E-6 2.73E-6	4.79E-6 1.27E-5	1.65E-5 3.58E-5	
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.509 C 0.736 1.280 1.037 0.727 0.815	2.740 1.871 2.309 2.153 1.429 1.291	2.412 1.929 2.342 2.008 1.304 1.286	2.422 1.953 2.347 2.096 1.392 1.266	1.210 2.013 2.268 1.972 1.249 1.047	0.538 0.882 1.610 0.662 0.784 0.220	0.289 0.194 1.138 0.026 0.180 0.225	85 105 103 87 82 99	86 107 104 95 95 95	31 112 96 84 74 49	1 13 32 -36 8 -73	-43 -74 -11 -98 -75 -72	4.55E-7 4.24E-6 5.24E-6 1.91E-6 2.32E-6 9.40E-7	1.07E-5 1.41E-5 5.52E-5 4.99E-6 1.25E-5 2.51E-6	> 1.00E-4 5.33E-5 > 1.00E-4 1.68E-5 4.97E-5 6.47E-6	

		Natio	onal	Cano	er Ir	nstitu In-	ute D Vitro	evelop Testii	omer ng R	ital T esult	hera s	peuti	cs Program	I	
NSC : D - 782	787 / 1				Exp	erimer	nt ID:1	501NS15	5			Test	Туре : 08	Units : N	1olar
Report Date :	Decemb	ber 27, 2	2015		Tes	t Date	: Janua	ary 12, 20	15			QNS	:	MC :	
COMI : KCN-F	PGJ-29				Sta	in Rea	gent : S	SRB Dual	-Pass I	Related	ł	SSPL	_ : 0ZAS		
	T :				0-1	L	og10 Cor	ncentration							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.717 0.653 0.199 0.703 1.023 0.437	2.224 1.845 1.304 2.348 2.377 1.718	2.284 1.859 1.262 2.363 2.503 1.665	2.306 1.759 1.258 2.285 2.491 1.699	1.871 1.726 1.159 2.143 2.418 1.538	0.672 0.628 0.267 0.721 0.832 0.405	0.415 0.460 0.191 0.534 0.587 0.327	104 101 96 101 109 96	105 93 96 96 108 99	77 90 87 87 103 86	-6 -4 6 1 -19 -7	-42 -30 -4 -24 -43 -25	2.09E-6 2.67E-6 2.86E-6 2.72E-6 2.73E-6 2.43E-6	8.38E-6 9.10E-6 3.89E-5 1.10E-5 7.02E-6 8.33E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	Cancer 0.479 0.760 0.811 1.204 1.302 0.666 0.626 0.184 1.034	1.581 2.286 2.226 1.534 2.343 1.975 1.854 1.997 2.215	1.533 2.250 2.160 1.468 2.230 1.946 1.771 2.006 2.060	1.605 2.073 2.076 1.474 2.304 1.879 1.764 2.041 2.083	1.635 2.190 2.276 1.579 2.432 1.896 1.656 2.021 2.006	0.467 1.083 0.626 0.827 0.625 0.494 0.730 0.126 0.219	0.136 0.004 0.072 0.032 0.051 0.170 0.080 0.061 0.049	96 98 95 80 89 98 93 100 87	102 86 89 96 93 93 102 89	105 94 104 114 108 94 84 101 82	-3 21 -23 -31 -52 -26 8 -32 -79	-72 -100 -91 -97 -96 -75 -87 -67 -95	3.24E-6 4.00E-6 2.65E-6 2.75E-6 2.31E-6 2.33E-6 2.81E-6 2.43E-6 1.59E-6	9.46E-6 1.50E-5 6.59E-6 6.08E-6 4.74E-6 6.09E-6 1.22E-5 5.79E-6 3.24E-6	4.86E-5 3.89E-5 2.50E-5 9.71E-6 3.13E-5 4.08E-5 3.30E-5 6.62E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.622 1.230 0.356 0.304 0.284 0.491 0.296	2.030 3.361 2.334 2.044 1.576 2.883 2.220	1.987 3.278 2.373 2.018 1.610 2.855 2.233	1.966 3.420 2.346 2.031 1.745 2.948 2.246	2.166 3.394 2.082 1.856 1.782 2.509 2.180	0.377 0.138 0.107 0.184 0.077 0.304 0.333	0.143 0.065 0.011 -0.004 -0.010 0.123 0.125	97 96 102 99 103 99 101	95 103 101 99 113 103 101	110 102 87 89 116 84 98	-39 -89 -70 -40 -73 -38 2	-77 -95 -97 -100 -100 -75 -58	2.51E-6 1.87E-6 2.02E-6 2.23E-6 1.91E-6 3.16E-6	5.44E-6 3.42E-6 3.59E-6 4.92E-6 4.11E-6 4.89E-6 1.08E-5	1.91E-5 6.26E-6 7.47E-6 1.48E-5 7.55E-6 2.10E-5 7.41E-5
CNS Cancer SF-268 SF-295 SNB-19 SNB-75 U251	0.582 1.038 1.209 0.966 0.375	2.229 3.338 2.863 1.951 1.526	2.194 3.267 2.715 1.782 1.526	2.172 3.209 2.779 1.727 1.553	2.006 3.375 2.816 1.731 1.505	0.748 0.696 1.988 1.433 0.310	0.173 0.020 0.168 -0.008 0.030	98 97 91 83 100	97 94 95 77 102	86 102 97 78 98	10 -33 47 47 -17	-70 -98 -86 -100 -92	3.00E-6 2.42E-6 8.75E-6 8.20E-6 2.61E-6	1.33E-5 5.69E-6 2.26E-5 2.10E-5 7.08E-6	5.58E-5 1.83E-5 5.35E-5 4.58E-5 2.73E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.205 0.783 0.484 0.515 1.113 0.575 0.773 0.918 0.535	1.501 1.784 1.852 2.679 1.909 1.952 2.797 1.558 2.019	1.452 1.740 1.833 2.657 1.941 1.936 2.780 1.519 1.873	1.364 1.782 1.735 2.530 1.903 1.800 2.695 1.531 1.796	0.895 1.713 1.744 2.468 1.878 1.878 1.888 2.745 1.474 1.762	0.040 0.629 0.486 0.409 0.906 0.337 0.090 0.711 0.271	0.005 0.274 0.095 0.030 0.100 0.107 -0.009 0.101 0.116	96 99 99 104 99 99 99 94 90	89 100 91 93 99 89 95 96 85	53 93 90 96 95 97 87 83	-81 -20 -21 -19 -41 -88 -23 -49	-98 -65 -94 -91 -81 -100 -89 -78	1.06E-6 2.40E-6 2.87E-6 2.30E-6 2.52E-6 2.15E-6 2.15E-6 2.17E-6 1.77E-6	2.50E-6 6.69E-6 1.00E-5 6.51E-6 6.88E-6 4.98E-6 3.34E-6 6.22E-6 4.22E-6	5.90E-6 4.67E-5 4.19E-5 2.51E-5 2.71E-5 1.63E-5 6.22E-6 2.59E-5 1.05E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.704 0.402 0.615 0.803 0.565 0.709 1.189	2.427 1.446 1.467 2.134 1.815 2.295 2.310	2.418 1.456 1.418 2.111 1.788 2.320 2.285	2.486 1.449 1.386 2.022 1.807 2.282 2.246	2.321 1.360 1.356 2.262 1.743 2.209 2.386	0.706 0.372 0.857 1.056 0.597 0.840 1.421	0.264 -0.015 0.128 0.264 0.101 0.332 -0.022	99 101 94 98 98 102 98	103 100 90 92 99 99 99	94 92 87 110 94 95 107	-7 28 19 3 8 21	-63 -100 -79 -67 -82 -53 -100	2.94E-6 2.63E-6 4.27E-6 4.55E-6 3.04E-6 3.28E-6 4.57E-6	1.00E-5 8.41E-6 1.84E-5 1.66E-5 1.07E-5 1.36E-5 1.48E-5	6.31E-5 2.88E-5 5.35E-5 6.32E-5 4.17E-5 8.86E-5 3.85E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.746 1.555 0.519 0.577 0.951 0.597 0.974 0.674	2.386 2.459 2.263 3.008 1.576 2.074 1.778 2.539	2.375 2.349 2.280 2.973 1.593 1.985 1.700 2.479	2.241 2.257 2.230 2.903 1.609 1.990 1.775 2.465	2.518 2.534 2.222 2.988 1.651 2.067 1.934 2.426	0.452 1.794 0.093 0.259 0.226 0.451 0.955 0.275	0.018 0.024 0.035 -0.020 0.058 0.183 -0.030 0.154	99 88 101 99 103 94 90 97	91 78 98 96 105 94 100 96	108 108 98 99 112 100 119 94	-39 26 -82 -55 -76 -24 -2 -59	-98 -98 -93 -100 -94 -69 -100 -77	2.47E-6 5.16E-6 1.84E-6 2.08E-6 2.51E-6 3.73E-6 1.94E-6	5.40E-6 1.63E-5 3.49E-6 4.39E-6 3.94E-6 6.35E-6 9.64E-6 4.11E-6	1.52E-5 4.09E-5 6.63E-6 9.25E-6 7.25E-6 3.71E-5 3.09E-5 8.71E-6
Prostate Cancer PC-3 DU-145	0.505 0.451	1.773 2.182	1.797 2.283	1.802 2.161	1.787 1.942	0.374 0.710	0.111 -0.024	102 106	102 99	101 86	-26 15	-78 -100	2.52E-6 3.22E-6	6.24E-6 1.35E-5	2.89E-5 3.67E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.509 C 0.736 1.280 1.037 0.727 0.815	2.670 1.838 2.347 2.232 1.564 1.297	2.539 1.844 2.274 2.224 1.535 1.267	2.386 1.840 2.290 2.126 1.440 1.275	2.034 1.981 2.365 2.217 1.498 1.202	0.720 0.951 1.745 0.761 0.932 0.361	0.211 0.232 1.035 0.004 0.277 0.180	94 101 93 99 96 94	87 100 95 91 85 95	71 113 102 99 92 80	10 20 44 -27 24 -56	-59 -69 -19 -100 -62 -78	2.18E-6 4.72E-6 7.74E-6 2.45E-6 4.19E-6 1.67E-6	1.39E-5 1.67E-5 4.95E-5 6.13E-6 1.92E-5 3.89E-6	7.47E-5 6.16E-5 > 1.00E-4 2.09E-5 7.27E-5 9.08E-6

		Nati	onal	Cano	er Ir	nstitu In-	ıte D ∙Vitro	evelop Testii	omer ng R	ital T esult	hera s	peuti	cs Progran	า	
NSC : D - 782	290 / 1				Exp	erimer	nt ID:1	411NS92	2			Test	Туре : 08	Units : N	Iolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Nove	mber 17,	2014			QNS	:	MC :	
COMI : KCN-F	PGJ-24				Sta	in Rea	gent : S	RB Dual	Pass I	Related	1	SSPL	: 0ZAS		
						L	og10 Cor	ncentration							
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	optica -6.0	I Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.751 1.087 0.254 0.707 1.107 0.407	2.375 2.948 1.846 2.424 2.440 1.914	2.463 2.856 1.831 2.366 2.495 1.864	2.452 2.697 1.721 2.370 2.588 1.766	1.478 2.486 1.055 2.237 1.603 0.714	0.639 1.173 0.373 0.726 0.990 0.441	0.399 0.765 0.322 0.641 0.750 0.317	105 95 99 97 104 97	105 87 92 97 111 90	45 75 50 89 37 20	-15 5 7 -11 2	-47 -30 4 -9 -32 -22	8.17E-7 2.27E-6 1.02E-6 2.78E-6 6.71E-7 3.76E-7	5.61E-6 1.36E-5 > 1.00E-4 1.28E-5 6.01E-6 1.23E-5	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	Cancer 0.445 0.746 0.707 1.182 1.082 0.534 0.583 0.277 0.927	2.007 2.092 1.789 1.725 2.423 1.743 1.491 2.109 2.333	2.046 1.954 1.656 1.724 2.473 1.653 1.456 2.252 2.256	2.060 2.030 1.770 1.723 2.495 1.672 1.436 2.254 2.211	1.879 1.935 1.508 1.703 2.321 1.538 1.240 1.884 1.874	0.514 1.065 0.663 0.986 0.964 0.393 0.452 0.241 0.236	0.092 0.015 0.070 0.043 0.624 0.136 0.076 0.091 0.170	102 90 88 100 104 92 96 108 95	103 95 98 100 105 94 108 91	92 88 74 96 92 83 72 88 67	4 -6 -17 -26 -23 -13 -75	-79 -98 -90 -96 -42 -75 -87 -67 -82	3.01E-6 3.92E-6 1.99E-6 2.56E-6 2.57E-6 2.00E-6 1.72E-6 2.37E-6 1.33E-6	1.13E-5 1.56E-5 8.35E-6 7.12E-6 7.84E-6 5.74E-6 5.79E-6 7.40E-6 2.98E-6	4.46E-5 4.03E-5 3.32E-5 2.62E-5 > 1.00E-4 3.09E-5 2.67E-5 4.79E-5 6.71E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.428 0.481 0.302 0.242 0.237 0.407 0.228	1.407 1.639 2.332 1.575 1.307 1.906 1.335	1.352 1.578 2.272 1.435 1.306 1.852 1.341	1.433 1.495 2.357 1.423 1.390 1.760 1.353	1.139 1.618 0.740 1.021 0.726 1.051 0.739	0.140 0.020 0.077 0.200 0.116 0.293 0.200	0.058 0.020 -0.002 0.049 0.099 0.094 0.120	94 95 97 90 100 96 101	103 88 101 89 108 90 102	73 98 22 58 46 43 46	-67 -96 -75 -18 -51 -28 -12	-87 -96 -100 -80 -58 -77 -48	1.45E-6 1.77E-6 4.40E-7 1.29E-6 8.53E-7 7.09E-7 8.51E-7	3.30E-6 3.20E-6 1.68E-6 5.87E-6 2.97E-6 4.03E-6 6.16E-6	7.51E-6 5.80E-6 5.56E-6 3.31E-5 9.75E-6 2.81E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.550 0.846 0.872 0.613 1.282 0.474	1.753 2.831 2.686 2.078 2.484 1.909	1.694 2.601 2.515 2.099 2.155 1.951	1.658 2.818 2.616 2.082 2.235 1.913	1.596 2.657 2.375 1.888 2.225 1.374	0.675 0.924 0.749 0.812 1.932 0.269	0.204 0.133 0.123 0.142 0.653 0.004	95 88 91 101 73 103	92 99 96 100 79 100	87 91 83 87 78 63	10 4 -14 14 54 -43	-63 -84 -86 -77 -49 -99	3.04E-6 2.97E-6 2.18E-6 3.19E-6 1.09E-5 1.32E-6	1.39E-5 1.11E-5 7.14E-6 1.41E-5 3.34E-5 3.91E-6	6.65E-5 4.08E-5 3.16E-5 5.04E-5 > 1.00E-4 1.32E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.257 0.719 0.552 0.574 1.289 0.759 0.737 1.349 1.253	1.699 1.162 2.085 2.052 2.251 2.050 2.694 2.622 3.062	1.647 1.152 2.068 1.947 2.246 2.016 2.764 2.607 3.017	1.513 1.143 2.160 1.974 2.215 2.041 2.750 2.624 3.157	0.543 1.174 1.895 1.267 2.192 1.958 2.449 2.472 3.006	0.037 0.676 0.603 0.124 1.081 0.354 0.029 1.162 0.756	0.025 0.184 0.107 0.020 0.260 0.093 0.025 0.085 0.207	96 98 99 100 97 104 99 98	87 96 105 95 96 99 103 100 105	20 103 88 47 94 93 87 88 97	-86 -6 3 -78 -16 -53 -96 -14 -40	-90 -74 -81 -97 -80 -88 -97 -94 -84	3.56E-7 3.05E-6 2.79E-6 8.62E-7 2.50E-6 1.96E-6 1.60E-6 2.37E-6 2.20E-6	1.54E-6 8.81E-6 1.10E-5 2.37E-6 7.13E-6 4.31E-6 3.00E-6 7.31E-6 5.12E-6	4.58E-6 4.39E-5 4.31E-5 5.93E-6 3.40E-5 9.48E-6 5.61E-6 2.84E-5 1.72E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.897 0.322 0.726 0.685 0.542 0.506 0.813	2.435 1.158 1.465 1.525 2.015 1.692 1.738	2.447 1.160 1.351 1.383 2.066 1.647 1.653	2.528 1.108 1.391 1.450 2.197 1.583 1.742	2.437 0.561 1.226 1.576 1.429 1.123 1.706	0.952 0.052 0.812 0.431 0.627 0.476 1.033	0.268 -0.001 0.154 0.103 0.037 0.355 -0.014	101 100 85 83 103 96 91	106 94 90 91 112 91 100	100 29 68 106 60 52 97	4 -84 12 -37 6 -6 24	-70 -100 -79 -85 -93 -30 -100	3.30E-6 4.71E-7 2.07E-6 2.46E-6 1.54E-6 1.08E-6 4.36E-6	1.12E-5 1.79E-6 1.35E-5 5.51E-6 1.14E-5 7.90E-6 1.56E-5	5.32E-5 4.99E-6 4.80E-5 1.86E-5 3.66E-5 > 1.00E-4 3.94E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.566 1.333 0.614 0.634 0.869 1.046 0.898	2.059 1.720 2.468 2.581 1.331 2.858 2.215 2.455	2.064 1.711 2.353 2.272 1.331 2.874 2.185 2.244	2.132 1.769 2.438 2.413 1.395 2.826 2.207 2.256	0.966 1.854 1.938 1.850 1.284 2.531 2.161 2.045	0.246 0.364 0.234 0.100 0.072 0.924 0.902 0.144	0.028 0.071 0.077 0.007 0.074 0.236 0.049 0.091	100 98 94 84 100 101 97 86	105 113 98 91 109 98 99 87	27 135 71 62 93 84 95 74	-57 -73 -62 -84 -89 3 -14 -84	-95 -95 -88 -99 -88 -73 -95 -90	5.04E-7 2.56E-6 1.45E-6 1.22E-6 2.60E-6 2.60E-6 2.61E-6 1.41E-6	2.09E-6 4.46E-6 3.43E-6 2.67E-6 3.26E-6 1.09E-5 7.48E-6 2.93E-6	8.33E-6 7.77E-6 8.13E-6 5.84E-6 6.14E-6 4.99E-5 2.78E-5 6.08E-6
Prostate Cancer PC-3 DU-145	0.477 0.365	1.663 1.325	1.636 1.357	1.658 1.300	1.441 1.124	0.269 0.581	0.117 0.011	98 103	100 97	81 79	-44 23	-75 -97	1.78E-6 3.27E-6	4.47E-6 1.54E-5	1.58E-5 4.04E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T T-47D MDA-MB-468	0.321 0.677 1.447 0.742 0.682	1.733 1.500 2.239 1.452 1.305	1.543 1.551 2.172 1.347 1.290	1.571 1.560 2.256 1.420 1.302	0.611 1.531 2.262 1.319 1.125	0.380 0.642 1.600 0.779 0.251	0.178 0.203 1.092 0.242 0.177	87 106 92 85 98	89 107 102 95 100	20 104 103 81 71	4 -5 19 5 -63	-45 -70 -25 -67 -74	3.68E-7 3.12E-6 4.29E-6 2.57E-6 1.43E-6	1.22E-5 8.95E-6 2.76E-5 1.18E-5 3.38E-6	> 1.00E-4 4.90E-5 > 1.00E-4 5.76E-5 7.97E-6

		Natio	onal	Cano	er Ir	nstitu In-	ite De Vitro	evelop Testir	omer ng R	ital T esult	hera s	peutio	cs Progran	n	
NSC : D - 782	291 / 1				Exp	erimer	nt ID:1	411NS92	2			Test	Гуре : 08	Units : N	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Nover	mber 17,	2014			QNS	:	MC :	
COMI : KCN-F	PGJ-25				Sta	in Rea	gent : S	RB Dual	Pass I	Related	ł	SSPL	: 0ZAS		
					0.11	Lo	og10 Cor	centration							
Panel/Cell Line	Zero	Ctrl	-8.0	Mear -7.0	-6.0	-5.0	es -4.0	-8.0	-7.0	ercent G -6.0	-5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.751 1.087 0.254 0.707 1.107 0.407	2.488 3.037 1.858 2.539 2.542 1.951	2.538 2.996 1.812 2.441 2.574 1.901	2.553 2.950 1.745 2.503 2.677 1.882	2.201 2.829 1.646 2.335 2.464 1.788	0.730 1.139 0.423 0.761 1.012 0.456	0.476 0.797 0.248 0.565 0.693 0.312	103 98 97 95 102 97	104 96 93 98 109 96	83 89 87 89 95 89	-3 3 11 3 -9 3	-37 -27 -3 -20 -37 -23	2.44E-6 2.84E-6 3.04E-6 2.83E-6 2.70E-6 2.87E-6	9.26E-6 1.23E-5 6.38E-5 1.34E-5 8.25E-6 1.32E-5	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	Cancer 0.445 0.746 0.707 1.182 1.082 0.534 0.583 0.277 0.927	1.984 2.068 1.736 1.690 2.406 1.724 1.552 2.113 2.271	2.010 1.954 1.624 1.691 2.472 1.670 1.462 2.141 2.205	2.003 2.002 1.709 1.674 2.511 1.620 1.488 2.233 2.166	1.977 1.989 1.807 1.740 2.500 1.602 1.439 2.125 2.047	1.001 1.549 0.723 1.377 0.803 0.551 0.759 0.209 0.446	0.216 0.264 0.149 0.055 1.008 0.242 0.085 0.146 0.151	102 91 89 100 105 95 91 101 95	101 95 97 108 91 93 106 92	100 94 107 110 107 90 88 101 83	36 61 2 38 -26 1 18 -25 -52	-52 -65 -79 -95 -7 -55 -86 -47 -84	6.04E-6 1.22E-5 3.47E-6 6.87E-6 2.69E-6 2.69E-6 3.51E-6 2.53E-6 1.76E-6	2.58E-5 3.05E-5 1.05E-5 6.39E-6 1.06E-5 1.50E-5 6.35E-6 4.13E-6	9.60E-5 7.65E-5 4.37E-5 4.58E-5 > 1.00E-4 8.25E-5 4.54E-5 > 1.00E-4 9.68E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.428 0.481 0.302 0.242 0.237 0.407 0.228	1.375 1.552 2.285 1.488 1.331 1.904 1.227	1.284 1.534 2.253 1.389 1.383 1.861 1.197	1.376 1.553 2.232 1.450 1.379 1.811 1.264	1.462 1.622 2.399 1.337 1.465 1.677 1.345	0.338 0.081 0.168 0.295 0.218 0.311 0.332	0.074 0.057 0.031 0.069 0.146 0.110 0.115	90 98 92 105 97 97	100 100 97 97 104 94 104	109 106 106 88 112 85 112	-21 -83 -44 4 -8 -24 10	-83 -88 -90 -71 -38 -73 -50	2.85E-6 1.99E-6 2.35E-6 2.84E-6 3.29E-6 2.09E-6 4.07E-6	6.89E-6 3.64E-6 5.06E-6 1.14E-5 8.54E-6 6.05E-6 1.49E-5	2.94E-5 6.69E-6 1.33E-5 5.20E-5 > 1.00E-4 3.41E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.550 0.846 0.872 0.613 1.282 0.474	1.784 2.739 2.588 2.068 2.475 1.926	1.749 2.523 2.459 2.085 2.182 1.911	1.685 2.616 2.552 2.137 2.216 1.962	1.662 2.718 2.619 2.045 2.252 1.841	0.889 1.102 1.292 1.045 2.075 0.621	0.281 0.199 0.153 0.164 1.236 0.032	97 89 92 101 75 99	92 94 98 105 78 102	90 99 102 98 81 94	27 14 24 30 66 10	-49 -76 -82 -73 -4 -93	4.37E-6 3.74E-6 4.68E-6 5.06E-6 1.72E-5 3.35E-6	2.29E-5 1.41E-5 1.69E-5 1.94E-5 8.88E-5 1.25E-5	<pre>> 1.00E-4 5.08E-5 4.97E-5 5.95E-5 > 1.00E-4 3.81E-5</pre>
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.257 0.719 0.552 0.574 1.289 0.759 0.737 1.349 1.253	1.736 1.202 2.022 1.990 2.262 2.141 2.686 2.567 3.036	1.708 1.166 2.031 1.869 2.267 2.024 2.674 2.556 3.057	1.586 1.159 2.093 1.931 2.271 2.044 2.807 2.638 3.123	1.288 1.242 2.007 1.830 2.158 2.088 2.655 2.539 3.011	0.118 0.902 0.731 0.528 1.539 0.682 0.271 1.656 0.941	0.046 0.213 0.123 0.111 0.309 0.103 0.022 0.264 0.230	98 93 101 91 100 91 99 99 101	90 91 105 96 101 93 106 106 105	70 108 99 89 99 96 98 98 99	-54 38 12 -8 26 -10 -63 25 -25	-82 -70 -78 -81 -76 -86 -97 -80 -82	1.44E-6 6.71E-6 3.67E-6 2.51E-6 4.14E-6 2.72E-6 1.99E-6 4.54E-6 2.48E-6	3.66E-6 2.23E-5 1.37E-5 8.26E-6 1.79E-5 8.02E-6 4.06E-6 1.73E-5 6.29E-6	9.27E-6 6.47E-5 4.91E-5 5.55E-5 3.33E-5 8.28E-6 5.15E-5 2.77E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-4 OVCAR-8 NCI/ADR-RES SK-OV-3	0.897 0.322 0.726 0.685 0.542 0.506 0.813	2.534 1.180 1.484 1.515 2.034 1.667 1.748	2.499 1.199 1.421 1.355 2.039 1.631 1.683	2.493 1.162 1.418 1.412 2.094 1.616 1.774	2.484 1.114 1.398 1.607 2.086 1.603 1.788	1.520 0.394 0.916 1.203 0.777 0.639 1.158	0.309 0.011 0.112 0.202 0.164 0.378 0.436	98 102 92 81 100 97 93	97 98 91 88 104 96 103	97 92 89 111 103 95 104	38 8 25 62 16 11 37	-66 -97 -85 -71 -70 -25 -46	6.26E-6 3.19E-6 4.05E-6 1.24E-5 4.07E-6 3.43E-6 6.38E-6	2.33E-5 1.20E-5 1.69E-5 2.95E-5 1.53E-5 2.05E-5 2.77E-5	7.07E-5 3.59E-5 4.83E-5 7.00E-5 5.88E-5 > 1.00E-4 > 1.00E-4
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.566 1.333 0.614 0.634 0.631 0.869 1.046 0.898	2.085 1.761 2.387 2.511 1.325 2.864 2.216 2.484	2.134 1.696 2.256 2.406 1.336 2.891 2.223 2.246	2.107 1.755 2.356 2.390 1.374 2.833 2.175 2.315	2.229 1.921 2.374 2.509 1.388 2.789 2.341 2.390	0.523 1.771 0.632 0.911 0.471 1.138 1.390 0.687	0.058 0.216 0.094 0.040 0.050 0.569 0.057 0.135	103 85 93 94 102 101 101 85	101 99 98 94 107 98 96 89	109 137 99 100 109 96 111 94	-8 102 15 -25 13 29 -23	-90 -84 -85 -94 -92 -35 -95 -85	3.22E-6 1.91E-5 3.17E-6 3.86E-6 2.75E-6 3.62E-6 5.58E-6 2.37E-6	8.61E-6 3.55E-5 1.03E-5 1.37E-5 6.47E-6 1.91E-5 1.73E-5 6.31E-6	3.28E-5 6.58E-5 3.94E-5 3.95E-5 2.34E-5 > 1.00E-4 4.37E-5 2.70E-5
Prostate Cancer PC-3 DU-145	0.477 0.365	1.565 1.321	1.648 1.340	1.689 1.310	1.736 1.286	0.510 0.670	0.118 0.016	108 102	111 99	116 96	3 32	-75 -96	3.83E-6 5.24E-6	1.09E-5 1.78E-5	4.75E-5 4.39E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T T-47D MDA-MB-468	0.321 0.677 1.447 0.742 0.682	1.613 1.521 2.423 1.470 1.335	1.403 1.558 2.331 1.346 1.305	1.495 1.510 2.402 1.399 1.336	1.239 1.567 2.417 1.345 1.253	0.521 0.924 2.175 0.930 0.564	0.187 0.248 1.542 0.229 0.240	84 104 90 83 95	91 99 98 90 100	71 105 99 83 87	15 29 75 26 -17	-42 -63 10 -69 -65	2.39E-6 5.34E-6 2.39E-5 3.76E-6 2.28E-6	1.86E-5 2.07E-5 > 1.00E-4 1.87E-5 6.83E-6	> 1.00E-4 7.16E-5 > 1.00E-4 6.28E-5 4.87E-5

		Natio	onal (Cano	er Ir	nstitu In-	ite Do Vitro	evelop Testir	mer ng R	ital T esult	hera s	peutic	s Progra	m	
NSC : D - 782	135 / 1				Exp	erimer	nt ID:1	410NS77	,			Test T	ype : 08	Units : N	lolar
Report Date :	Decemb	ber 27, 2	2015		Tes	t Date	: Octob	oer 27, 20	14			QNS :		MC :	
COMI : KCN-F	PGJ-8				Sta	in Rea	gent : S	RB Dual-	Pass	Related	1	SSPL	: 0ZAS		
						Lo	og10 Cor	ncentration				•		•	
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	n Optica -6.0	I Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.340 0.973 0.334 0.644 0.758 0.284	1.492 3.302 2.631 2.367 2.666 1.690	1.566 3.271 2.706 2.338 2.771 1.590	1.526 3.178 2.588 2.320 2.796 1.494	0.464 1.841 0.636 1.344 0.963 0.458	0.378 0.709 0.368 0.573 0.773 0.293	0.263 0.574 0.329 0.488 0.552 0.309	106 99 103 98 106 93	103 95 98 97 107 86	11 37 13 41 11 12	3 -27 -11 -11 1	-23 -41 -2 -24 -27 2	3.75E-7 6.00E-7 3.68E-7 6.82E-7 3.90E-7 3.09E-7	1.34E-5 3.79E-6 2.97E-5 6.10E-6 1.06E-5 > 1.00E-4	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	Cancer 0.444 0.724 0.644 1.250 1.157 0.578 1.071 0.190 1.254	1.726 1.877 1.835 1.734 2.475 1.817 2.352 2.213 2.626	1.699 1.751 1.731 1.710 2.551 1.809 2.364 2.351 2.510	1.745 1.800 1.778 1.738 2.434 1.689 2.254 2.332 2.492	1.604 1.609 1.437 1.713 2.052 1.542 2.110 1.636 1.599	0.404 0.464 0.506 0.899 0.478 0.236 0.838 0.266 0.263	0.074 0.029 0.165 0.115 0.513 0.140 0.066 0.105 0.095	98 89 91 95 106 99 101 107 92	101 93 95 101 97 90 92 106 90	90 77 96 68 78 81 71 25	-9 -36 -21 -28 -59 -59 -22 4 -79	-83 -96 -74 -91 -56 -76 -94 -45 -92	2.55E-6 1.73E-6 1.54E-6 2.34E-6 1.39E-6 1.60E-6 2.00E-6 2.08E-6 4.15E-7	8.10E-6 4.80E-6 5.71E-6 5.93E-6 3.44E-6 3.70E-6 6.14E-6 1.19E-5 1.74E-6	3.55E-5 1.71E-5 3.46E-5 2.24E-5 8.54E-6 8.56E-6 2.46E-5 > 1.00E-4 5.26E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.558 0.701 0.520 0.225 0.422 0.465 0.239	2.019 2.304 3.141 1.574 1.942 3.039 2.241	1.912 2.387 3.105 1.489 1.960 3.034 2.301	2.076 2.342 3.014 1.437 2.001 3.017 2.388	1.324 2.306 0.239 0.417 0.590 1.847 0.729	0.292 0.053 0.064 0.157 0.131 0.369 0.313	0.169 0.066 0.017 0.063 0.145 0.149 0.147	93 105 99 94 101 100 103	104 102 95 90 104 99 107	52 100 -54 14 11 54 24	-48 -92 -88 -30 -69 -21 4	-70 -91 -97 -72 -66 -68 -39	1.06E-6 1.82E-6 2.01E-7 3.36E-7 3.80E-7 1.12E-6 4.92E-7	3.34E-6 3.31E-6 4.34E-7 2.08E-6 1.37E-6 5.26E-6 1.22E-5	1.28E-5 6.02E-6 9.40E-7 2.94E-5 5.80E-6 4.16E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.518 0.944 1.012 0.799 0.973 0.760	1.809 2.916 2.758 2.466 1.966 2.335	1.769 2.694 2.648 2.486 1.849 2.423	1.705 2.862 2.793 2.493 1.899 2.410	1.487 2.652 1.771 1.990 1.825 1.852	0.603 0.661 0.325 0.890 1.313 0.258	0.233 0.090 0.090 0.209 0.126 0.030	97 89 94 101 88 106	92 97 102 102 93 105	75 87 43 71 86 69	7 -30 -68 5 34 -66	-55 -90 -91 -74 -87 -96	2.32E-6 2.06E-6 7.73E-7 2.11E-6 4.94E-6 1.39E-6	1.28E-5 5.53E-6 2.46E-6 1.17E-5 1.91E-5 3.25E-6	8.29E-5 2.14E-5 6.90E-6 5.00E-5 4.95E-5 7.61E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.293 0.805 0.473 0.492 1.312 0.623 1.114 1.117 0.587	2.040 1.726 1.911 2.701 2.364 1.776 3.030 2.126 2.511	2.116 1.658 1.792 2.409 2.305 1.728 3.072 2.114 2.420	1.876 1.626 1.779 2.499 2.259 1.796 3.060 2.155 2.374	0.208 1.519 1.033 1.048 2.127 1.163 2.438 1.927 0.728	0.072 0.505 0.256 0.564 0.726 0.324 0.075 0.735 0.378	0.055 0.134 0.124 0.151 0.225 0.081 0.027 0.079 0.250	104 93 92 87 94 96 102 99 95	91 89 91 90 102 102 103 93	-29 77 39 25 77 47 69 80 7	-76 -37 -46 3 -45 -48 -93 -34 -36	-81 -83 -74 -69 -83 -87 -98 -93 -57	2.19E-7 1.73E-6 6.12E-7 4.19E-7 1.68E-6 8.74E-7 1.31E-6 1.84E-6 3.17E-7	5.72E-7 4.73E-6 2.87E-6 1.11E-5 4.31E-6 3.12E-6 2.66E-6 5.02E-6 1.48E-6	2.82E-6 1.88E-5 1.39E-5 5.41E-5 1.38E-5 1.13E-5 5.41E-6 1.86E-5 4.56E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.881 0.472 0.677 0.725 0.604 0.586 0.850	2.509 1.866 1.744 2.084 2.247 1.918 1.715	2.463 1.951 1.609 1.941 2.248 2.012 1.633	2.526 1.919 1.653 2.124 2.197 1.922 1.712	2.070 0.893 1.426 1.078 0.755 0.827 1.759	0.385 0.325 0.968 0.432 0.633 0.523 1.073	0.219 0.039 0.172 0.148 0.102 0.533 0.035	97 106 87 89 100 107 91	101 104 91 103 97 100 100	73 30 70 26 9 18 105	-56 -31 27 -40 2 -11 26	-75 -92 -75 -80 -83 -9 -96	1.51E-6 5.38E-7 2.96E-6 4.87E-7 3.43E-7 4.09E-7 4.95E-6	3.67E-6 3.10E-6 1.85E-5 2.46E-6 1.05E-5 4.23E-6 1.63E-5	8.93E-6 2.05E-5 5.74E-5 1.76E-5 4.07E-5 > 1.00E-4 4.20E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.788 1.169 0.537 0.594 1.270 0.664 0.886 0.987	2.686 2.021 2.259 2.782 1.787 2.526 1.865 2.576	2.514 2.111 2.555 1.760 2.563 1.798 2.347	2.613 2.180 2.300 2.576 1.810 2.625 1.827 2.367	1.152 2.193 0.193 1.881 1.704 1.203 1.636 1.774	0.096 0.124 0.091 0.937 0.115 0.485 0.505 0.071	0.059 0.014 0.058 0.109 0.031 0.177 0.024 0.060	91 111 95 90 95 102 93 86	96 119 102 91 104 105 96 87	19 120 -64 59 84 29 77 50	-88 -89 -83 16 -91 -27 -43 -93	-93 -99 -89 -82 -98 -73 -97 -94	3.98E-7 2.16E-6 2.06E-7 1.60E-6 1.56E-6 5.30E-7 1.67E-6 9.71E-7	1.51E-6 3.74E-6 4.12E-7 1.45E-5 3.02E-6 3.29E-6 4.37E-6 2.23E-6	4.43E-6 6.49E-6 8.23E-7 4.73E-5 5.83E-6 3.13E-5 1.34E-5 5.00E-6
Prostate Cancer PC-3 DU-145	0.736 0.413	1.759 1.733	1.678 1.711	1.735 1.716	1.418 1.162	0.430 0.652	0.168 0.029	92 98	98 99	67 57	-42 18	-77 -93	1.42E-6 1.49E-6	4.12E-6 1.46E-5	1.72E-5 4.10E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.396 0.568 0.973 1.343 0.680 0.703	2.015 1.413 1.991 2.679 1.379 1.346	1.759 1.504 1.954 2.540 1.250 1.340	1.805 1.538 2.034 2.613 1.291 1.280	0.786 1.171 2.015 1.855 1.103 0.948	0.373 0.633 1.291 0.755 0.710 0.154	0.181 0.186 0.923 0.037 0.238 0.103	84 111 96 90 82 99	87 115 104 95 87 90	24 71 102 38 61 38	-6 8 31 -44 4 -78	-54 -67 -5 -97 -65 -85	3.87E-7 2.16E-6 5.44E-6 6.23E-7 1.54E-6 5.88E-7	6.39E-6 1.26E-5 7.22E-5 2.93E-6 1.15E-5 2.13E-6	8.16E-5 5.88E-5 > 1.00E-4 1.31E-5 6.07E-5 5.73E-6

		Natio	onal (Cano	er Ir	nstitu In-	ite De Vitro	evelop Testir	men ng R	ital T esult	hera s	peutic	s Prograr	n	
NSC : D - 782	134 / 1				Exp	erimer	nt ID:1	410NS77	,			Test T	ype : 08	Units : N	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Octob	er 27, 20	14			QNS :		MC :	
COMI : KCN-F	PGJ-7				Sta	in Rea	gent : S	RB Dual	Pass I	Related	I	SSPL	: 0ZAS		
						Lo	og10 Cor	centration							
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	n Optica -6.0	l Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.340 0.973 0.334 0.644 0.758 0.284	1.586 3.278 2.658 2.340 2.727 1.617	1.659 3.227 2.684 2.416 2.740 1.518	1.632 3.188 2.654 2.270 2.807 1.483	1.300 2.994 2.414 2.097 2.398 1.219	0.426 0.808 0.435 0.668 0.768 0.307	0.256 0.592 0.404 0.448 0.544 0.266	106 98 101 104 101 93	104 96 100 96 104 90	77 88 90 86 83 70	7 -17 4 1 2	-25 -39 3 -30 -28 -6	2.43E-6 2.29E-6 2.91E-6 2.65E-6 2.52E-6 1.97E-6	1.65E-5 6.89E-6 > 1.00E-4 1.11E-5 1.04E-5 1.62E-5	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.444 0.724 0.644 1.250 1.157 0.578 1.071 0.190 1.254	1.647 1.813 1.713 1.734 2.469 1.885 2.425 2.135 2.505	1.635 1.683 1.576 1.705 2.510 1.841 2.343 2.250 2.414	1.618 1.686 1.648 1.719 2.609 1.819 2.283 2.265 2.465	1.649 1.661 1.646 1.774 2.515 1.781 2.355 2.075 2.299	0.500 1.033 0.384 1.541 0.587 0.423 1.363 0.184 0.547	0.131 0.122 0.159 0.115 1.133 0.178 0.072 0.105 0.219	99 88 87 94 103 97 94 106 93	98 88 94 97 111 95 89 107 97	100 86 94 108 104 92 95 97 84	5 28 -40 60 -49 -27 22 -3 -56	-71 -83 -75 -91 -2 -69 -93 -45 -83	3.35E-6 4.22E-6 2.12E-6 1.17E-5 2.24E-6 2.26E-6 4.09E-6 2.94E-6 1.74E-6	1.15E-5 1.80E-5 5.00E-6 2.50E-5 4.76E-6 5.95E-6 1.54E-5 9.25E-6 3.95E-6	5.32E-5 5.04E-5 1.88E-5 5.37E-5 > 1.00E-4 3.51E-5 4.20E-5 > 1.00E-4 9.00E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.558 0.701 0.520 0.225 0.422 0.465 0.239	1.939 2.278 3.183 1.506 2.002 2.971 2.148	1.833 2.278 3.117 1.380 1.989 2.923 2.161	1.965 2.198 3.183 1.413 2.038 2.993 2.250	1.940 2.268 2.896 1.144 2.023 2.667 1.918	0.398 0.080 0.097 0.142 0.279 0.572 0.389	0.205 0.065 0.031 0.042 0.237 0.166 0.154	92 100 97 90 99 98 101	102 95 100 93 102 101 105	100 99 89 72 101 88 88	-29 -89 -81 -37 -34 4 8	-63 -91 -94 -81 -44 -64 -36	2.45E-6 1.83E-6 1.70E-6 1.58E-6 2.40E-6 2.84E-6 2.98E-6	5.99E-6 3.38E-6 3.33E-6 4.57E-6 5.62E-6 1.15E-5 1.52E-5	4.14E-5 6.23E-6 6.54E-6 1.97E-5 > 1.00E-4 6.19E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.518 0.944 1.012 0.799 0.973 0.760	1.759 2.852 2.736 2.503 1.919 2.284	1.693 2.707 2.596 2.506 1.688 2.315	1.688 2.759 2.717 2.521 1.817 2.343	1.692 2.748 2.634 2.481 1.830 2.305	0.848 0.724 0.518 1.539 1.484 0.957	0.291 0.230 0.106 0.197 0.599 0.088	95 92 92 100 76 102	94 95 99 101 89 104	95 95 94 99 91 101	27 -23 -49 43 54 13	-44 -76 -90 -75 -38 -88	4.53E-6 2.39E-6 2.03E-6 7.60E-6 1.10E-5 3.81E-6	2.39E-5 6.34E-6 4.55E-6 2.32E-5 3.84E-5 1.34E-5	> 1.00E-4 3.23E-5 1.07E-5 6.12E-5 > 1.00E-4 4.18E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.293 0.805 0.473 0.492 1.312 0.623 1.114 1.117 0.587	2.093 1.734 1.868 2.492 2.343 1.875 3.005 2.051 2.526	2.093 1.608 1.731 2.414 2.276 1.685 2.983 1.998 2.401	1.946 1.601 1.784 2.455 2.298 1.853 3.057 2.004 2.476	1.524 1.640 1.633 2.357 2.211 1.765 2.914 1.930 2.122	0.065 0.701 0.369 0.762 1.716 0.513 0.337 1.089 0.422	0.033 0.192 0.094 0.225 0.376 0.142 0.063 0.090 0.229	100 86 90 93 85 99 94 94	92 86 94 98 96 98 103 95 97	68 90 83 93 87 91 95 87 79	-78 -13 -22 13 39 -18 -70 -3 -28	-89 -76 -80 -54 -71 -77 -94 -92 -61	1.34E-6 2.44E-6 2.06E-6 3.49E-6 5.96E-6 2.39E-6 1.88E-6 2.59E-6 1.87E-6	2.93E-6 7.48E-6 6.17E-6 1.58E-5 2.26E-5 6.87E-6 3.78E-6 9.36E-6 5.46E-6	6.44E-6 3.85E-5 3.03E-5 8.65E-5 6.41E-5 3.49E-5 7.59E-6 3.39E-5 4.60E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.881 0.472 0.677 0.725 0.604 0.586 0.850	2.505 1.797 1.598 2.071 2.161 2.024 1.621	2.514 1.820 1.495 1.895 2.177 2.044 1.536	2.550 1.869 1.544 2.036 2.202 2.016 1.611	2.426 1.798 1.409 2.179 2.086 1.953 1.640	0.984 0.635 0.916 0.686 0.709 0.719 1.067	0.215 0.013 0.207 0.122 0.116 0.548 0.576	101 102 89 87 101 101 89	103 105 94 97 103 99 99	95 100 80 108 95 95 102	6 12 26 -5 7 9 28	-76 -97 -69 -83 -81 -7 -32	3.22E-6 3.72E-6 3.55E-6 3.25E-6 3.24E-6 3.35E-6 5.08E-6	1.20E-5 1.29E-5 1.87E-5 8.95E-6 1.19E-5 3.83E-5 2.92E-5	4.87E-5 3.70E-5 6.26E-5 3.74E-5 4.44E-5 > 1.00E-4 > 1.00E-4
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.788 1.169 0.537 0.594 1.270 0.664 0.886 0.987	2.713 1.966 2.267 2.580 1.824 2.539 1.889 2.682	2.583 2.030 2.119 2.334 1.816 2.572 1.854 2.439	2.680 2.096 2.286 2.478 1.875 2.643 1.836 2.415	2.670 2.079 2.114 2.388 1.911 2.508 1.972 2.440	0.223 1.879 0.158 0.775 0.374 0.516 0.851 0.170	0.022 0.178 0.102 0.140 0.070 0.221 0.053 0.080	93 108 91 88 99 102 97 86	98 116 101 95 109 106 95 84	98 114 91 90 116 98 108 86	-72 89 -71 9 -71 -22 -4 -83	-97 -85 -81 -77 -95 -67 -94 -92	1.91E-6 1.68E-5 1.80E-6 3.14E-6 2.25E-6 2.52E-6 3.31E-6 1.63E-6	3.77E-6 3.25E-5 3.66E-6 1.28E-5 4.18E-6 6.53E-6 9.22E-6 3.23E-6	7.45E-6 6.31E-5 7.46E-6 4.90E-5 7.76E-6 4.20E-5 3.25E-5 6.39E-6
Prostate Cancer PC-3 DU-145	0.736 0.413	1.698 1.603	1.674 1.597	1.793 1.618	1.783 1.513	0.707 0.674	0.298 0.003	97 99	110 101	109 92	-4 22	-60 -99	3.32E-6 4.00E-6	9.23E-6 1.52E-5	6.74E-5 3.92E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.396 C 0.568 0.973 1.343 0.680 0.703	2.087 1.471 1.903 2.705 1.275 1.342	1.844 1.490 1.861 2.567 1.228 1.353	1.840 1.481 1.938 2.697 1.267 1.416	1.027 1.495 1.908 2.638 1.180 1.276	0.424 0.694 1.421 1.072 0.698 0.388	0.141 0.192 1.028 0.039 0.257 0.203	86 102 96 90 92 102	85 101 104 99 99 112	37 103 101 95 84 90	2 14 48 -20 3 -45	-64 -66 -97 -62 -71	5.44E-7 3.92E-6 9.24E-6 2.63E-6 2.63E-6 1.97E-6	1.06E-5 1.49E-5 > 1.00E-4 6.68E-6 1.11E-5 4.64E-6	6.05E-5 6.28E-5 > 1.00E-4 2.44E-5 6.50E-5 1.58E-5

Developmental Ther	apeutics Program	NSC: D-783633 / 1	Conc: 1.00E-5 Molar	Test Date: Mar 16, 2015
One Dose Mea	an Graph	Experiment ID: 1503	OS51	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Per	cent
Panel/Cell Line Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 SR Non-Small Cell Lung Cancer A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H23 NCI-H322M NCI-H322M NCI-H322M NCI-H322Z Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer SF-268 SF-295 SF-295 SF-539 SNB-19 SNB-75 U251 Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-28	Growth Percent 18.92 94.32 49.12 74.61 20.79 82.19 120.49 109.33 107.79 93.31 107.79 93.31 102.95 102.95 102.39 96.01 101.53 84.08 60.13 77.22 96.75 101.43 89.92 96.47 85.96 13.39 131.33 88.47 98.75 93.09 96.31 94.31 72.31 79.28 95.95 97.68 144.19 95.88 104.61 116.29 119.94 103.41 106.65 101.67 109.52 67.28 113.28 100.07	Mean Growth	Percent - Growth Perc	
Kange				
	150	100 50	0 -50	-100 -150

		Natio	onal	Cano	er Ir	nstitu In-	ite D ∙Vitro	evelop Testir	men ng R	ital T esult	hera s	peutio	cs Progran	n	
NSC : D - 783	634 / 1				Exp	erimer	nt ID:1	504NS69)			Test	Туре : 08	Units : N	lolar
Report Date :	Decemb	ber 27, 2	2015		Tes	t Date	: April	13, 2015				QNS	:	MC :	
COMI : KCN-F	PGJ-40				Sta	in Rea	gent : S	RB Dual	Pass I	Related	1	SSPL	: 0ZAS		
						L	og10 Cor	ncentration				•			
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	optica -6.0	I Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.574 1.047 0.333 0.964 0.812 0.493	2.008 2.957 1.944 3.024 2.821 1.666	1.928 2.856 2.004 2.988 2.706 1.545	1.900 2.846 1.957 2.906 2.758 1.477	0.982 2.626 1.134 2.706 2.253 1.002	0.482 0.741 0.336 0.715 0.725 0.352	0.368 0.581 0.235 0.637 0.500 0.301	94 95 104 98 94 90	92 94 101 94 97 84	28 83 50 85 72 43	-16 -29 -26 -11 -29	-36 -45 -29 -34 -38 -39	4.61E-7 1.96E-6 9.86E-7 2.06E-6 1.83E-6 6.86E-7	4.36E-6 5.48E-6 1.01E-5 5.83E-6 7.40E-6 4.01E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	Cancer 0.453 0.829 0.638 1.340 0.894 0.626 1.234 0.444 0.866	1.770 2.048 1.659 1.934 2.228 1.939 2.734 3.088 1.932	1.761 2.033 1.626 1.840 2.193 1.888 2.653 3.120 1.804	1.847 1.967 1.566 1.854 2.108 1.891 2.676 3.114 1.935	1.955 2.060 1.711 1.966 2.157 1.849 2.733 3.128 1.703	0.487 1.414 0.632 1.466 0.536 0.500 1.684 0.595 0.411	0.071 -0.022 0.089 0.073 0.407 0.125 0.082 0.116 0.187	99 99 97 84 97 96 95 101 88	106 93 91 86 91 96 96 101 100	114 101 105 95 93 100 102 79	3 48 -21 -40 -20 30 6 -53	-84 -100 -86 -95 -55 -80 -93 -74 -78	3.75E-6 9.14E-6 3.31E-6 4.54E-6 2.14E-6 2.40E-6 5.17E-6 3.45E-6 1.65E-6	1.07E-5 2.11E-5 9.80E-6 1.52E-5 5.04E-6 6.63E-6 1.75E-5 1.18E-5 3.97E-6	4.03E-5 4.59E-5 3.77E-5 4.12E-5 4.85E-5 3.15E-5 4.45E-5 5.01E-5 9.55E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.359 0.425 0.319 0.264 0.380 0.437 0.686	1.545 1.348 2.657 1.933 1.762 2.320 3.149	1.496 1.440 2.701 1.860 1.782 2.344 3.127	1.463 1.407 2.579 1.784 1.886 2.336 3.112	1.317 1.519 1.013 1.791 1.737 1.939 3.076	0.216 0.025 0.179 0.229 0.262 0.190 0.640	0.087 0.025 0.022 0.001 0.139 0.081 0.200	96 110 102 96 101 101 99	93 106 97 91 109 101 98	81 119 30 91 98 80 97	-40 -94 -44 -13 -31 -57 -7	-76 -94 -93 -100 -63 -81 -71	1.80E-6 2.10E-6 4.98E-7 2.49E-6 2.36E-6 1.65E-6 2.84E-6	4.66E-6 3.61E-6 2.53E-6 7.47E-6 3.74E-6 3.84E-6 8.60E-6	1.90E-5 6.20E-6 1.32E-5 2.66E-5 3.83E-5 8.94E-6 4.72E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.763 0.867 1.112 0.565 0.683 0.592	2.305 2.585 2.958 2.127 1.615 2.105	2.312 2.488 2.913 2.043 1.510 2.076	2.291 2.414 2.758 2.065 1.452 2.084	2.278 2.549 2.846 2.050 1.462 2.082	1.025 0.838 1.251 0.991 1.066 0.621	0.187 0.086 0.103 0.186 -0.003 0.031	100 94 95 89 98	99 90 89 96 83 99	98 98 94 95 84 98	17 -3 8 27 41 2	-75 -90 -91 -67 -100 -95	3.92E-6 2.97E-6 3.22E-6 4.62E-6 6.17E-6 3.18E-6	1.53E-5 9.27E-6 1.19E-5 1.94E-5 1.96E-5 1.05E-5	5.30E-5 3.45E-5 3.85E-5 6.58E-5 4.42E-5 3.44E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.331 0.800 0.432 0.305 1.421 0.745 0.820 0.990 1.140	2.273 1.486 1.892 1.894 2.566 2.362 3.110 1.898 3.117	2.126 1.524 1.875 1.827 2.585 2.325 3.063 1.884 3.064	1.965 1.474 1.763 1.723 2.600 2.228 3.026 1.931 3.053	0.684 1.451 1.670 1.572 2.513 2.200 3.040 2.053 3.033	0.056 0.776 0.402 0.232 1.898 0.494 0.061 0.893 1.064	0.020 0.172 0.061 -0.001 0.241 0.128 -0.002 0.066 0.221	92 106 99 96 102 98 98 98 98 97	84 98 91 89 103 92 96 104 97	18 95 80 95 90 97 117 96	-83 -3 -24 42 -34 -93 -10 -7	-94 -79 -86 -100 -83 -83 -100 -93 -81	3.29E-7 2.87E-6 2.39E-6 1.93E-6 6.99E-6 2.10E-6 1.77E-6 3.38E-6 2.80E-6	1.51E-6 9.31E-6 8.38E-6 5.86E-6 2.16E-5 5.34E-6 3.25E-6 8.36E-6 8.60E-6	4.70E-6 4.19E-5 3.50E-5 5.43E-5 5.43E-5 5.96E-6 3.02E-5 3.85E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.843 0.780 0.904 0.923 0.542 0.634 0.795	2.789 2.345 2.195 1.972 2.186 2.218 1.976	2.753 2.381 2.241 1.915 2.109 2.241 1.959	2.771 2.442 2.055 1.859 2.202 2.099 1.893	2.675 2.298 2.002 1.956 2.204 2.141 1.975	1.021 0.802 1.278 0.988 0.566 0.791 1.250	0.161 0.006 0.012 0.276 0.075 0.484 0.004	98 102 104 95 95 101 99	99 106 89 89 101 92 93	94 97 85 98 101 95 100	9 1 29 6 1 10 38	-81 -99 -99 -70 -86 -24 -100	3.31E-6 3.10E-6 4.21E-6 3.35E-6 3.26E-6 3.38E-6 6.49E-6	1.26E-5 1.03E-5 1.69E-5 1.21E-5 1.04E-5 1.97E-5 1.90E-5	4.54E-5 3.24E-5 4.16E-5 5.45E-5 3.86E-5 > 1.00E-4 4.38E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.666 1.313 0.539 0.830 0.803 0.980 0.909 0.988	2.458 1.986 2.193 3.282 1.573 3.229 1.683 2.805	2.366 1.785 2.154 3.208 1.538 3.170 1.563 2.734	2.342 1.842 2.098 3.129 1.543 3.190 1.578 2.770	2.409 1.919 2.158 3.126 1.550 3.241 1.676 2.647	0.771 1.846 0.193 1.191 0.166 1.535 1.374 0.168	0.051 0.037 0.086 0.024 0.031 0.377 0.017 0.050	95 70 98 97 95 97 85 96	94 79 94 96 98 86 98	97 90 98 94 97 101 99 91	6 79 -64 15 -79 25 60 -83	-92 -97 -84 -97 -96 -62 -98 -95	3.29E-6 1.46E-5 1.97E-6 3.57E-6 4.64E-6 1.16E-5 1.73E-6	1.15E-5 2.81E-5 4.02E-6 1.35E-5 3.55E-6 1.93E-5 2.40E-5 3.34E-6	3.70E-5 5.40E-5 8.17E-6 3.79E-5 6.82E-6 7.35E-5 4.96E-5 6.47E-6
Prostate Cancer PC-3 DU-145	0.571 0.326	2.258 1.468	2.224 1.511	2.215 1.437	2.228 1.401	0.616 0.435	0.133 0.006	98 104	97 97	98 94	3 10	-77 -98	3.20E-6 3.32E-6	1.08E-5 1.23E-5	4.60E-5 3.57E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.400 C 0.732 1.372 1.210 0.770 0.790	2.041 1.860 2.388 2.743 1.620 1.446	1.951 1.836 2.319 2.752 1.559 1.428	1.881 1.917 2.337 2.678 1.503 1.443	1.594 2.040 2.285 2.728 1.540 1.420	0.521 1.089 1.620 1.140 0.972 0.434	0.177 0.223 0.906 0.007 0.299 0.213	95 98 93 101 93 97	90 105 95 96 86 100	73 116 90 99 91 96	7 32 24 -6 24 -45	-56 -70 -34 -99 -61 -73	2.23E-6 6.06E-6 4.06E-6 2.94E-6 4.05E-6 2.12E-6	1.31E-5 2.05E-5 2.62E-5 8.81E-6 1.90E-5 4.79E-6	8.07E-5 6.41E-5 > 1.00E-4 2.96E-5 7.38E-5 1.50E-5

		Natio	onal	Cano	er Ir	nstitu In-	ite Do Vitro	evelop Testir	men ng R	ital T esult	hera s	peutic	s Progran	n	
NSC : D - 783	635 / 1				Exp	erimer	nt ID:1	504NS69)			Test 1	ype : 08	Units : M	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: April '	13, 2015				QNS		MC :	
COMI : KCN-F	PGJ-41				Sta	in Rea	gent : S	RB Dual-	Pass I	Related	1	SSPL	: 0ZAS		
						Lo	og10 Cor	ncentration							
Panel/Cell Line	Time Zero	Ctrl	-8.0	Mear -7.0	Optica -6.0	l Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.574 1.047 0.333 0.964 0.812 0.493	2.097 3.089 2.083 3.101 2.891 1.691	1.931 3.107 2.126 3.089 2.831 1.443	1.749 3.161 1.897 3.069 2.894 1.310	0.664 0.864 0.285 1.670 0.887 0.440	0.438 0.663 0.203 0.546 0.608 0.280	0.421 0.483 0.165 0.563 0.555 0.293	89 101 102 99 97 79	77 104 89 98 100 68	6 -18 -15 33 4 -11	-24 -37 -39 -43 -25 -43	-27 -54 -51 -42 -32 -41	2.40E-7 2.77E-7 2.39E-7 5.51E-7 3.31E-7 1.70E-7	1.58E-6 7.17E-7 7.24E-7 2.71E-6 1.33E-6 7.31E-7	> 1.00E-4 5.96E-5 8.87E-5 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	Cancer 0.453 0.829 0.638 1.340 0.894 0.626 1.234 0.444 0.866	1.891 2.084 1.638 1.896 2.269 1.936 2.790 3.137 1.800	1.851 2.030 1.645 1.841 2.183 1.864 2.771 3.141 1.704	1.890 1.957 1.744 1.907 2.108 1.889 2.794 3.176 1.671	0.894 1.529 1.167 1.904 1.077 1.279 2.951 3.074 0.752	0.187 0.097 0.379 0.749 0.356 0.320 1.529 0.381 0.339	0.079 -0.016 0.045 0.119 0.553 0.205 0.150 0.197 0.260	97 96 101 90 94 95 99 100 90	100 90 111 102 88 96 100 101 86	31 56 53 101 13 50 110 98 -13	-59 -88 -41 -44 -60 -49 19 -14 -61	-83 -100 -93 -91 -38 -67 -88 -56 -70	5.26E-7 1.10E-6 1.07E-6 2.25E-6 3.24E-7 9.93E-7 4.57E-6 2.67E-6 2.31E-7	2.20E-6 2.44E-6 3.68E-6 4.97E-6 1.52E-6 3.20E-6 1.50E-5 7.45E-6 7.37E-7	7.97E-6 5.42E-6 1.51E-5 1.33E-5 1.15E-5 4.42E-5 7.27E-5 5.92E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.359 0.425 0.319 0.264 0.380 0.437 0.686	1.529 1.361 2.697 1.968 1.717 2.284 3.197	1.561 1.346 2.551 1.861 1.810 2.279 3.162	1.416 1.509 1.895 1.706 1.752 2.190 3.135	0.376 0.240 0.112 0.249 0.301 0.383 1.391	0.129 0.039 0.012 0.031 0.090 0.112 0.250	0.126 0.059 0.018 0.030 0.123 0.091 0.266	103 98 94 94 107 100 99	90 116 66 85 103 95 98	1 -44 -65 -6 -21 -12 28	-64 -91 -96 -88 -76 -74 -64	-65 -86 -95 -89 -68 -79 -61	2.84E-7 2.59E-7 1.33E-7 2.42E-7 2.67E-7 2.62E-7 4.83E-7	1.05E-6 5.33E-7 3.20E-7 8.65E-7 6.77E-7 7.67E-7 2.02E-6	6.10E-6 1.37E-6 7.68E-7 3.43E-6 3.35E-6 4.05E-6 7.11E-6
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.763 0.867 1.112 0.565 0.683 0.592	2.337 2.679 2.977 2.123 1.602 2.174	2.342 2.516 2.998 2.059 1.527 2.092	2.373 2.521 2.866 2.104 1.437 2.019	1.782 1.952 1.736 1.524 1.239 0.888	0.382 0.198 0.698 0.252 0.102 0.080	0.086 0.036 0.105 0.191 0.038 0.040	100 91 101 96 92 95	102 91 94 99 82 90	65 60 33 62 60 19	-50 -77 -37 -55 -85 -86	-89 -96 -91 -66 -95 -93	1.34E-6 1.18E-6 5.33E-7 1.25E-6 1.18E-6 3.65E-7	3.67E-6 2.73E-6 2.97E-6 3.36E-6 2.60E-6 1.51E-6	1.00E-5 6.33E-6 1.73E-5 8.98E-6 5.74E-6 4.50E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.331 0.800 0.432 0.305 1.421 0.745 0.820 0.990 1.140	2.133 1.557 1.896 1.992 2.478 2.364 3.096 2.013 3.071	2.005 1.622 1.793 1.877 2.520 2.303 3.047 1.875 3.016	1.656 1.581 1.596 1.782 2.540 2.211 2.925 1.858 3.049	0.096 1.223 0.445 0.284 2.313 1.164 1.142 1.680 1.960	0.023 0.577 0.120 0.148 0.706 0.214 0.195 0.397 0.487	0.039 0.213 0.071 0.053 0.203 0.120 0.018 0.113 0.172	93 109 93 93 104 96 98 86 97	74 103 79 88 106 91 92 85 99	-71 56 1 -7 84 26 14 67 42	-93 -28 -72 -52 -50 -71 -76 -60 -57	-88 -73 -84 -83 -86 -84 -98 -89 -89 -85	1.45E-7 1.18E-6 2.37E-7 2.50E-7 1.80E-6 4.24E-7 3.48E-7 1.37E-6 7.35E-7	3.23E-7 4.65E-6 1.03E-6 8.45E-7 4.23E-6 1.43E-6 3.39E-6 2.66E-6	7.16E-7 3.06E-5 4.95E-6 9.19E-6 9.94E-6 6.03E-6 5.12E-6 8.36E-6 8.45E-6
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.843 0.780 0.904 0.923 0.542 0.634 0.795	2.753 2.401 2.111 2.003 2.240 2.197 1.965	2.877 2.382 2.168 2.010 2.142 2.229 1.951	2.859 2.564 1.966 1.978 2.130 2.068 1.908	1.753 1.022 1.539 1.705 0.747 0.866 1.840	0.570 0.056 0.115 0.435 0.434 0.722 0.716	0.293 0.029 0.028 0.187 0.103 0.538 0.007	106 99 105 101 94 102 99	106 110 88 98 93 92 95	48 15 53 72 12 15 89	-32 -93 -87 -53 -20 6 -10	-65 -96 -97 -80 -81 -15 -99	9.10E-7 4.28E-7 1.04E-6 1.51E-6 3.42E-7 3.49E-7 2.49E-6	3.93E-6 1.38E-6 2.38E-6 3.78E-6 2.37E-6 1.87E-5 7.94E-6	3.42E-5 4.00E-6 5.41E-6 9.48E-6 3.10E-5 > 1.00E-4 2.81E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.666 1.313 0.539 0.830 0.803 0.980 0.909 0.988	2.396 2.119 2.221 3.269 1.583 3.194 1.593 2.886	2.379 1.932 2.228 3.194 1.637 3.171 1.601 2.814	2.379 1.959 2.096 3.073 1.580 3.269 1.671 2.775	1.450 2.110 0.164 1.432 1.021 1.664 1.431 1.909	0.074 0.108 0.088 0.207 0.082 0.781 0.208 0.095	0.007 0.044 0.107 0.034 0.059 0.206 0.010 0.111	99 77 100 97 107 99 101 96	99 80 93 92 100 103 111 94	45 99 -70 25 28 31 76 49	-89 -92 -84 -75 -90 -20 -77 -90	-99 -97 -80 -96 -93 -79 -99 -89	8.18E-7 1.81E-6 1.83E-7 4.20E-7 4.92E-7 5.45E-7 1.48E-6 9.29E-7	2.18E-6 3.30E-6 3.72E-7 1.77E-6 1.73E-6 4.01E-6 3.14E-6 2.23E-6	5.13E-6 6.04E-6 7.57E-7 5.60E-6 4.59E-6 3.20E-5 6.65E-6 5.12E-6
Prostate Cancer PC-3 DU-145	0.571 0.326	2.269 1.497	2.242 1.515	2.275 1.491	1.101 0.454	0.279 0.031	0.115 0.017	98 102	100 99	31 11	-51 -91	-80 -95	5.35E-7 3.62E-7	2.39E-6 1.28E-6	9.66E-6 3.98E-6
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.400 0.732 1.372 1.210 0.770 0.790	2.061 1.762 2.458 2.688 1.643 1.469	1.736 1.840 2.310 2.706 1.530 1.424	1.536 1.832 2.374 2.601 1.540 1.401	0.983 1.406 2.403 1.915 1.356 1.127	0.110 0.626 1.317 0.134 0.640 0.229	0.195 0.215 1.033 0.013 0.486 0.184	80 108 86 101 87 93	68 107 92 94 88 90	35 65 95 48 67 50	-73 -14 -4 -89 -17 -71	-51 -71 -25 -99 -37 -77	3.56E-7 1.56E-6 2.84E-6 8.90E-7 1.60E-6 9.76E-7	2.12E-6 6.59E-6 9.11E-6 2.23E-6 6.28E-6 2.58E-6	6.16E-6 4.29E-5 > 1.00E-4 5.19E-6 > 1.00E-4 6.69E-6

Developmental Ther	apeutics Program	NSC: D-782284 / 1	Conc: 1.00E-5 Molar	Test Date: Oct 20, 2014
One Dose Mea	an Graph	Experiment ID: 1410	OS79	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Perc	cent
Panel/Cell Line Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer A549/ATCC EKVX HOP-92 NCI-H226 NCI-H226 NCI-H322M NCI-H322M NCI-H322M NCI-H322 Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251 Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-28 SK-MEL-28 OVCAR-3 OVCAR-4 OVCAR-	Growth Percent 43.67 86.92 82.96 93.03 78.53 72.68 94.77 104.19 96.37 115.76 99.05 100.33 117.43 79.83 78.78 120.69 118.99 88.00 98.72 107.96 99.22 102.76 95.72 105.80 97.26 98.63 97.61 98.38 72.16 03.67 89.04 99.45 97.49 107.59 96.03 84.98 89.93 119.55 111.51 100.69 125.93 98.22 104.12 105.45 108.66 116.74 108.78	Mean Growth I	Percent - Growth Perc	
Mean Delta	98.44 54.77			
Range	82.26			
	150	100 50	0 -50	-100 -150

		Natio	onal	Cano	er Ir	nstitu In-	ite D Vitro	evelop Testii	omer ng R	ntal T esult	hera s	peutio	cs Prograr	n	
NSC : D - 782	285 / 1				Exp	erimer	nt ID:1	411NS92	2			Test	Туре : 08	Units : M	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Nove	mber 17,	2014			QNS	:	MC :	
COMI : KCN-	PGJ-19				Sta	in Rea	gent : S	RB Dual	-Pass I	Related	ł	SSPL	: 0ZAS		
	_					L	og10 Cor	ncentration							
Panel/Cell Line	Zero	Ctrl	-8.0	Mear -7.0	-6.0	-5.0	-4.0	-8.0	-7.0	ercent G -6.0	-5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.751 1.087 0.254 0.707 1.107 0.407	2.316 2.811 1.851 2.579 2.539 2.063	2.406 2.768 1.908 2.532 2.630 1.957	2.455 2.698 1.836 2.494 2.700 1.881	1.623 2.376 1.156 1.781 2.250 0.804	0.724 1.156 0.424 0.741 1.161 0.494	0.370 0.685 0.197 0.459 0.764 0.316	106 98 104 97 106 94	109 93 99 95 111 89	56 75 56 57 80 24	-4 4 11 2 4 5	-51 -37 -23 -35 -31 -22	1.25E-6 2.24E-6 1.38E-6 1.36E-6 2.46E-6 3.98E-7	8.70E-6 1.25E-5 2.09E-5 1.12E-5 1.28E-5 1.55E-5	9.65E-5 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.445 0.746 0.707 1.182 1.082 0.534 0.583 0.277 0.927	1.985 2.137 1.743 1.754 2.373 1.657 1.497 2.233 2.424	2.009 2.031 1.568 1.772 2.431 1.581 1.478 2.329 2.288	2.031 2.046 1.710 1.784 2.429 1.583 1.467 2.373 2.364	2.066 2.051 1.771 1.783 2.429 1.517 1.431 2.292 2.172	0.942 1.018 0.476 1.087 0.472 0.281 0.673 0.261 0.470	0.390 0.413 0.231 0.098 0.862 0.089 0.064 0.151 0.234	102 92 83 103 104 93 98 105 91	103 93 97 105 104 93 97 107 96	105 94 103 105 104 87 93 103 83	32 20 -33 -56 -47 10 -6 -49	-12 -45 -67 -92 -20 -83 -89 -45 -75	5.71E-6 3.89E-6 2.45E-6 3.07E-6 2.18E-6 1.90E-6 3.27E-6 3.07E-6 1.78E-6	5.26E-5 2.01E-5 5.73E-6 8.49E-6 4.46E-6 4.46E-6 1.26E-5 8.85E-6 4.24E-6	> 1.00E-4 > 1.00E-4 3.15E-5 3.17E-5 - 1.18E-5 > 1.00E-4 1.07E-5
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.428 0.481 0.302 0.242 0.237 0.407 0.228	1.395 1.471 2.495 1.526 1.315 1.987 1.338	1.372 1.456 2.387 1.426 1.330 1.950 1.379	1.420 1.437 2.461 1.445 1.278 1.899 1.395	1.324 1.586 1.133 1.281 1.237 1.785 0.812	0.273 0.057 0.120 0.220 0.162 0.329 0.213	0.088 0.030 0.029 0.053 0.106 0.085 0.084	98 99 95 92 101 98 104	103 97 98 94 96 94 105	93 112 38 81 93 87 53	-36 -88 -60 -9 -32 -19 -7	-79 -94 -90 -78 -55 -79 -63	2.14E-6 2.03E-6 6.31E-7 2.20E-6 2.21E-6 2.24E-6 1.11E-6	5.23E-6 3.62E-6 2.43E-6 7.89E-6 5.57E-6 6.59E-6 7.68E-6	2.08E-5 6.44E-6 7.83E-6 3.89E-5 5.98E-5 3.26E-5 5.84E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.550 0.846 0.872 0.613 1.282 0.474	1.873 2.814 2.673 2.027 2.360 1.974	1.802 2.466 2.522 2.029 2.154 2.021	1.742 2.755 2.590 2.071 2.253 2.005	1.755 2.763 2.610 2.017 2.241 1.827	0.819 1.050 0.875 1.027 2.096 0.389	0.378 0.340 0.189 0.166 1.404 0.029	95 82 92 100 81 103	90 97 95 103 90 102	91 97 96 99 89 90	20 10 29 76 -18	-31 -60 -78 -73 11 -94	3.81E-6 3.50E-6 3.04E-6 5.06E-6 2.50E-5 2.35E-6	2.47E-5 1.40E-5 1.00E-5 1.93E-5 > 1.00E-4 6.83E-6	<pre>> 1.00E-4 7.25E-5 4.36E-5 5.96E-5 > 1.00E-4 2.64E-5</pre>
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.257 0.719 0.552 0.574 1.289 0.759 0.737 1.349 1.253	1.674 1.152 2.133 2.032 2.309 2.172 2.656 2.588 3.021	1.597 1.116 2.104 1.915 2.347 2.064 2.652 2.545 3.038	1.543 1.080 2.157 2.000 2.297 2.132 2.618 2.672 3.089	0.611 1.139 2.084 1.882 2.307 2.058 2.624 2.579 2.992	0.068 0.568 0.626 0.360 1.340 0.593 0.269 1.392 0.758	0.035 0.287 0.215 0.156 0.685 0.154 0.155 0.590 0.299	95 92 98 92 104 92 100 97 101	91 83 101 98 99 97 98 107 104	25 97 90 100 92 98 99 98	-74 -21 5 -37 5 -22 -64 3 -40	-87 -60 -61 -73 -47 -80 -79 -56 -76	4.17E-7 2.50E-6 3.22E-6 2.05E-6 3.35E-6 2.33E-6 1.99E-6 3.27E-6 2.24E-6	1.79E-6 6.64E-6 1.18E-5 5.08E-6 1.25E-5 6.42E-6 4.05E-6 1.14E-5 5.17E-6	5.77E-6 5.52E-5 6.77E-5 > 1.00E-4 3.06E-5 8.24E-6 7.84E-5 1.93E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.897 0.322 0.726 0.685 0.542 0.506 0.813	2.482 1.239 1.473 1.529 2.066 1.632 1.700	2.380 1.212 1.383 1.433 2.066 1.613 1.658	2.442 1.216 1.405 1.388 2.139 1.617 1.722	2.383 0.919 1.363 1.532 1.872 1.585 1.758	0.906 0.271 0.943 0.716 0.580 0.596 1.239	0.281 0.031 0.057 0.174 0.559 0.522 0.645	94 97 88 89 100 98 95	97 98 91 83 105 99 102	94 65 85 100 87 96 106	1 -16 29 4 2 8 48	-69 -91 -92 -75 1 1 -21	2.95E-6 1.54E-6 4.24E-6 3.32E-6 2.75E-6 3.32E-6 9.25E-6	1.02E-5 6.35E-6 1.73E-5 1.11E-5 > 1.00E-4 > 1.00E-4 4.99E-5	5.37E-5 2.86E-5 4.48E-5 > 1.00E-4 > 1.00E-4 > 1.00E-4
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.566 1.333 0.614 0.634 0.631 0.869 1.046 0.898	2.235 1.823 2.397 2.518 1.302 2.792 2.320 2.426	2.299 1.846 2.279 2.370 1.322 2.746 2.258 2.235	2.231 1.799 2.376 2.368 1.326 2.790 2.220 2.210	2.289 1.819 2.361 2.496 1.293 2.731 2.273 2.141	0.454 1.562 0.214 0.684 0.189 0.767 1.316 0.316	0.116 0.233 0.075 0.072 0.183 0.416 0.088 0.180	104 105 93 92 103 98 95 88	100 95 99 92 104 100 92 86	103 99 98 99 99 97 96 81	-20 47 -65 3 -70 -12 21 -65	-80 -83 -88 -89 -71 -52 -92 -80	2.71E-6 8.68E-6 3.22E-6 1.94E-6 2.70E-6 4.13E-6 1.64E-6	6.91E-6 2.30E-5 3.99E-6 1.07E-5 3.84E-6 7.80E-6 1.54E-5 3.60E-6	3.21E-5 5.60E-5 8.07E-6 3.77E-5 7.60E-6 8.86E-5 4.27E-5 7.91E-6
Prostate Cancer PC-3 DU-145	0.477 0.365	1.497 1.452	1.484 1.453	1.474 1.437	1.414 1.384	0.401 0.662	0.149 0.052	99 100	98 99	92 94	-16 27	-69 -86	2.44E-6 4.55E-6	7.10E-6 1.74E-5	4.41E-5 4.83E-5
Breast Cancer MCF7 MDA-MB-231/ATC HS 578T T-47D MDA-MB-468	0.321 C 0.677 1.447 0.742 0.682	1.659 1.471 2.437 1.527 1.304	1.501 1.512 2.441 1.421 1.304	1.525 1.548 2.511 1.437 1.292	0.760 1.516 2.471 1.413 1.230	0.392 0.712 1.991 0.942 0.254	0.163 0.146 1.718 0.434 0.139	88 105 100 86 100	90 110 107 89 98	33 106 103 85 88	5 4 55 25 -63	-49 -78 27 -42 -80	5.00E-7 3.55E-6 1.51E-5 3.90E-6 1.79E-6	1.25E-5 1.13E-5 > 1.00E-4 2.40E-5 3.83E-6	<pre>> 1.00E-4 4.54E-5 > 1.00E-4 > 1.00E-4 8.22E-6</pre>

		Natio	onal	Cano	cer Ir	nstitu In-	ite D Vitro	evelop Testi	omer ng R	ital T esult	hera s	peuti	cs Program	l	
NSC : D - 782	286 / 1				Exp	erimer	nt ID:1	411NS92	2			Test	Туре : 08	Units : N	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Nove	mber 17,	2014			QNS	:	MC :	
COMI : KCN-	PGJ-20				Sta	in Rea	gent : S	SRB Dual	-Pass I	Related	ł	SSPI	_:0ZAS		
	T :				0	L	og10 Cor	ncentration							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.751 1.087 0.254 0.707 1.107 0.407	2.452 3.057 1.728 2.455 2.457 1.902	2.444 3.063 1.586 2.551 2.526 1.862	2.379 3.004 1.627 2.310 2.590 1.750	2.236 3.079 1.409 2.185 2.492 1.479	0.836 0.923 0.358 0.676 1.116 0.386	0.610 0.721 0.241 0.547 0.936 0.357	100 100 90 105 105 97	96 97 93 92 110 90	87 101 78 85 103 72	5 -15 7 -4 1 -5	-19 -34 -5 -23 -15 -12	2.84E-6 2.75E-6 2.50E-6 2.44E-6 3.28E-6 1.92E-6	1.62E-5 7.41E-6 3.79E-5 8.93E-6 1.10E-5 8.57E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H460 NCI-H522	g Cancer 0.445 0.746 0.707 1.182 1.082 0.534 0.583 0.277 0.927	1.957 2.071 1.740 1.753 2.323 1.639 1.495 2.111 2.193	1.916 2.054 1.715 1.671 2.253 1.628 1.436 2.113 2.110	1.887 2.009 1.667 1.689 2.300 1.573 1.543 2.170 2.195	1.946 2.072 1.849 1.728 2.348 1.558 1.375 2.258 2.074	1.405 0.974 1.140 1.579 1.337 0.664 0.858 0.627 0.531	0.178 0.001 0.138 0.099 0.840 0.137 0.065 0.199 0.134	97 99 98 86 94 99 94 100 93	95 93 89 98 94 105 103 100	99 100 111 95 102 93 87 108 91	63 17 42 69 21 12 30 19 -43	-60 -100 -92 -22 -74 -89 -28 -86	1.29E-5 4.02E-6 7.61E-6 1.32E-5 4.35E-6 3.37E-6 4.46E-6 4.49E-6 2.02E-6	3.27E-5 1.40E-5 2.20E-5 2.70E-5 3.01E-5 1.37E-5 1.79E-5 2.53E-5 4.78E-6	8.30E-5 3.75E-5 5.63E-5 5.52E-5 5.21E-5 4.71E-5 > 1.00E-4 1.48E-5
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.428 0.481 0.302 0.242 0.237 0.407 0.228	1.272 1.634 2.238 1.433 1.256 1.924 1.226	1.291 1.578 2.320 1.396 1.243 1.979 1.178	1.281 1.657 2.245 1.406 1.348 1.947 1.295	1.401 1.591 2.351 1.298 1.373 1.856 1.417	0.682 0.071 0.203 0.129 0.135 0.322 0.355	0.073 0.012 0.028 0.028 0.065 0.097 0.144	102 95 104 97 99 104 95	101 102 100 98 109 102 107	115 96 106 89 111 96 119	30 -85 -33 -47 -43 -21 13	-83 -98 -91 -88 -73 -76 -37	5.83E-6 1.80E-6 2.53E-6 1.93E-6 2.50E-6 2.46E-6 4.46E-6	1.84E-5 3.39E-6 5.79E-6 4.52E-6 5.27E-6 6.62E-6 1.80E-5	5.10E-5 6.39E-6 1.97E-5 1.20E-5 1.72E-5 3.36E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.550 0.846 0.872 0.613 1.282 0.474	1.831 2.770 2.666 1.919 2.489 1.921	1.758 2.603 2.606 1.848 2.345 1.851	1.782 2.650 2.621 1.884 2.162 1.864	1.763 2.780 2.653 1.888 2.462 1.860	0.948 0.762 1.036 1.044 2.272 0.695	0.226 0.051 0.102 0.143 0.723 0.005	94 91 95 88 95	96 94 97 97 73 96	95 101 99 98 98 98	31 -10 9 33 82 15	-59 -94 -88 -77 -44 -99	5.03E-6 2.87E-6 3.52E-6 5.45E-6 1.80E-5 3.70E-6	2.21E-5 8.13E-6 1.24E-5 2.00E-5 4.49E-5 1.36E-5	7.94E-5 3.00E-5 4.04E-5 5.70E-5 > 1.00E-4 3.73E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.257 0.719 0.552 0.574 1.289 0.759 0.737 1.349 1.253	1.634 1.192 2.089 1.972 2.185 2.145 2.682 2.479 2.920	1.620 1.167 2.006 1.928 2.105 2.160 2.611 2.412 2.878	1.562 1.143 2.066 1.853 2.188 2.036 2.563 2.372 2.885	1.275 1.161 2.080 1.810 2.144 2.101 2.510 2.444 2.924	0.073 0.942 0.792 0.355 1.548 0.790 0.116 1.948 0.697	0.016 0.260 0.275 0.064 0.248 0.148 0.015 0.155 0.336	99 95 97 91 101 96 94 97	95 89 91 100 92 94 91 98	74 93 99 88 95 97 91 97 100	-72 47 16 -38 29 2 -84 53 -44	-94 -64 -50 -89 -81 -81 -98 -89 -73	1.46E-6 8.66E-6 3.89E-6 4.82E-6 3.13E-6 1.72E-6 1.05E-5 2.23E-6	3.22E-6 2.66E-5 1.73E-5 4.99E-6 1.84E-5 1.06E-5 3.31E-6 2.37E-5 4.93E-6	7.10E-6 7.50E-5 9.94E-5 5.24E-5 4.28E-5 6.37E-6 5.34E-5 1.57E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.897 0.322 0.726 0.685 0.542 0.506 0.813	2.381 1.213 1.448 1.588 1.962 1.596 1.734	2.330 1.226 1.443 1.548 1.948 1.603 1.764	2.476 1.228 1.460 1.568 1.959 1.575 1.721	2.449 1.225 1.501 1.855 1.893 1.520 1.856	1.132 0.356 1.009 0.808 0.539 0.525 1.491	0.333 0.022 0.187 0.273 0.228 0.394 0.204	97 101 99 96 99 101 103	106 102 102 98 100 98 99	105 101 107 130 95 93 113	16 4 39 14 2 74	-63 -93 -74 -60 -58 -22 -75	4.12E-6 3.36E-6 6.93E-6 4.85E-6 2.96E-6 2.96E-6 1.44E-5	1.59E-5 1.09E-5 2.21E-5 1.53E-5 9.87E-6 1.18E-5 3.13E-5	6.85E-5 3.58E-5 6.11E-5 7.28E-5 7.27E-5 > 1.00E-4 6.79E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.566 1.333 0.614 0.634 0.631 0.869 1.046 0.898	2.155 1.882 2.437 2.498 1.233 2.653 2.229 2.368	1.993 1.758 2.364 2.401 1.232 2.588 2.163 2.199	2.138 1.818 2.318 2.375 1.246 2.687 2.219 2.194	2.252 1.942 2.423 2.471 1.317 2.733 2.209 2.232	0.860 1.883 0.132 0.779 0.637 0.800 1.396 0.621	0.086 0.154 0.079 0.016 0.088 0.508 0.040 0.098	90 77 96 95 100 96 94 88	99 88 93 93 102 102 99 88	106 111 99 99 114 105 98 91	19 100 -79 8 1 -8 30 -31	-85 -88 -87 -97 -86 -42 -96 -89	4.37E-6 1.84E-5 1.89E-6 3.43E-6 3.05E-6 5.04E-6 2.16E-6	1.51E-5 3.39E-5 3.61E-6 1.19E-5 1.03E-5 8.50E-6 1.72E-5 5.58E-6	4.60E-5 6.25E-5 6.91E-6 3.54E-5 3.85E-5 > 1.00E-4 4.29E-5 2.13E-5
Prostate Cancer PC-3 DU-145	0.477 0.365	1.576 1.338	1.624 1.379	1.655 1.359	1.744 1.374	0.473 0.929	0.170 0.014	104 104	107 102	115 104	58	-64 -96	3.64E-6 1.13E-5	9.81E-6 2.38E-5	5.92E-5 5.02E-5
Breast Cancer MCF7 MDA-MB-231/ATC HS 578T T-47D MDA-MB-468	0.321 C 0.677 1.447 0.742 0.682	1.642 1.490 2.363 1.402 1.247	1.582 1.489 2.205 1.370 1.212	1.561 1.483 2.383 1.332 1.259	1.375 1.610 2.439 1.363 1.282	0.569 0.903 2.003 1.076 0.804	0.113 0.332 1.190 0.097 0.288	95 100 83 95 94	94 99 102 89 102	80 115 108 94 106	19 28 61 51 22	-65 -51 -18 -87 -58	3.07E-6 5.55E-6 1.37E-5 1.01E-5 4.61E-6	1.68E-5 2.25E-5 5.94E-5 2.33E-5 1.87E-5	6.65E-5 9.72E-5 > 1.00E-4 5.39E-5 7.98E-5

		Natio	onal	Cano	er Ir	nstitu In-	ute D Vitro	evelop Testii	omer ng R	ital T esult	hera s	peutio	cs Progran	า	
NSC : D - 782	287 / 1				Exp	erimer	nt ID : 1	411NS92	2			Test	Туре : 08	Units : N	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Nove	mber 17,	2014			QNS	:	MC :	
COMI : KCN-F	PGJ-21				Sta	in Rea	gent : S	SRB Dual	-Pass I	Related	ł	SSPL	: 0ZAS		
	Time				0-1	Lo	og10 Cor	ncentration							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.751 1.087 0.254 0.707 1.107 0.407	2.412 3.172 1.805 2.367 2.368 1.903	2.337 3.184 1.502 2.478 2.448 1.907	2.343 3.129 1.798 2.354 2.411 1.809	2.251 3.209 1.510 2.133 2.402 1.770	0.692 0.930 0.283 0.657 0.996 0.394	0.464 0.809 0.183 0.576 0.815 0.327	95 101 80 107 106 100	96 98 100 99 103 94	90 102 81 86 103 91	-8 -14 2 -7 -10 -3	-38 -26 -28 -19 -26 -20	2.57E-6 2.79E-6 2.46E-6 2.43E-6 2.93E-6 2.73E-6	8.32E-6 7.51E-6 1.16E-5 8.39E-6 8.15E-6 9.22E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-82 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.445 0.746 0.707 1.182 1.082 0.534 0.583 0.277 0.927	1.930 2.077 1.707 1.708 2.366 1.596 1.538 2.126 2.184	1.945 2.071 1.643 1.673 2.349 1.598 1.598 2.138 2.180	1.904 1.991 1.596 1.684 2.388 1.610 1.528 2.188 2.178	1.998 2.097 1.772 1.746 2.420 1.589 1.418 2.290 2.152	1.271 1.056 0.744 1.442 1.064 0.560 0.775 0.448 0.262	0.147 0.022 0.103 0.198 0.486 0.148 0.046 0.134 0.047	101 100 94 93 99 100 100 101 101	98 94 89 95 102 101 99 103 100	105 102 107 107 104 99 87 109 97	56 23 4 -2 2 20 9 -72	-67 -97 -85 -83 -55 -72 -92 -52 -95	1.11E-5 4.56E-6 3.54E-6 9.77E-6 3.25E-6 3.23E-6 3.60E-6 3.90E-6 1.91E-6	2.84E-5 1.56E-5 1.10E-5 2.36E-5 9.64E-6 1.08E-5 1.51E-5 1.42E-5 3.77E-6	7.26E-5 4.00E-5 5.62E-5 8.02E-5 5.03E-5 4.21E-5 9.40E-5 7.44E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.428 0.481 0.302 0.242 0.237 0.407 0.228	1.285 1.545 2.111 1.485 1.220 1.939 1.243	1.327 1.564 2.402 1.434 1.290 1.995 1.258	1.293 1.626 2.416 1.424 1.333 1.975 1.272	1.414 1.804 2.344 1.381 1.359 1.895 1.381	0.505 0.089 0.152 0.152 0.048 0.312 0.339	0.076 0.001 0.024 0.027 0.009 0.101 0.162	105 102 116 96 107 104 101	101 108 117 95 112 102 103	115 124 113 92 114 97 114	9 -81 -50 -37 -80 -23 11	-82 -100 -92 -89 -96 -75 -29	4.10E-6 2.30E-6 2.44E-6 2.10E-6 2.14E-6 2.46E-6 4.16E-6	1.25E-5 4.02E-6 4.95E-6 5.13E-6 3.87E-6 6.39E-6 1.87E-5	4.43E-5 7.03E-6 1.02E-5 1.76E-5 7.01E-6 3.26E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.550 0.846 0.872 0.613 1.282 0.474	1.781 2.747 2.684 1.915 2.363 1.811	1.765 2.645 2.627 1.885 2.297 1.807	1.740 2.583 2.609 1.868 2.203 1.802	1.759 2.831 2.626 1.917 2.268 1.839	0.887 0.792 1.065 0.963 2.057 0.725	0.264 0.061 0.121 0.110 0.179 0.012	99 95 97 98 94 100	97 91 96 85 99	98 104 97 100 91 102	27 -6 11 27 72 19	-52 -93 -86 -82 -86 -98	4.79E-6 3.10E-6 3.49E-6 4.84E-6 1.37E-5 4.22E-6	2.21E-5 8.75E-6 1.29E-5 1.77E-5 2.85E-5 1.45E-5	9.44E-5 3.19E-5 4.23E-5 5.08E-5 5.91E-5 3.90E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.257 0.719 0.552 0.574 1.289 0.759 0.737 1.349 1.253	1.603 1.192 2.057 1.969 2.096 2.156 2.695 2.529 2.950	1.640 1.218 1.986 2.126 2.165 2.702 2.397 2.922	1.554 1.213 1.993 1.890 2.113 2.045 2.724 2.478 2.929	1.366 1.233 2.055 1.947 2.070 2.176 2.710 2.547 2.967	0.059 0.824 0.559 0.438 1.083 0.773 0.116 1.855 0.961	0.026 0.155 0.099 0.046 0.050 0.097 0.017 0.067 0.151	103 106 95 101 104 101 100 89 98	96 104 96 94 102 92 101 96 99	82 109 100 98 97 101 101 102 101	-77 22 -24 -16 1 -84 43 -23	-90 -78 -82 -92 -96 -87 -98 -95 -88	1.59E-6 4.76E-6 3.17E-6 2.49E-6 2.60E-6 3.25E-6 1.88E-6 7.55E-6 2.57E-6	3.28E-6 1.66E-5 1.01E-5 6.39E-6 7.21E-6 1.03E-5 3.50E-6 2.05E-5 6.49E-6	6.75E-6 5.21E-5 4.08E-5 2.42E-5 2.65E-5 3.79E-5 6.52E-6 4.71E-5 2.59E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.897 0.322 0.726 0.685 0.542 0.506 0.813	2.477 1.225 1.446 1.495 1.970 1.572 1.677	2.503 1.231 1.448 1.510 1.931 1.592 1.695	2.609 1.239 1.411 1.468 2.018 1.598 1.672	2.461 1.211 1.414 1.677 2.033 1.565 1.761	0.969 0.386 0.894 0.865 0.669 0.587 1.500	0.259 0.028 0.104 0.220 0.145 0.395 0.079	102 101 100 102 97 102 102	108 101 95 97 103 102 99	99 98 95 122 104 99 110	5 7 23 22 9 8 80	-71 -91 -86 -68 -73 -22 -90	3.30E-6 3.39E-6 4.27E-6 5.28E-6 3.71E-6 3.45E-6 1.49E-5	1.15E-5 1.18E-5 1.64E-5 1.76E-5 1.28E-5 1.80E-5 2.94E-5	5.26E-5 3.79E-5 4.71E-5 6.33E-5 5.20E-5 > 1.00E-4 5.79E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.566 1.333 0.614 0.634 0.631 0.869 1.046 0.898	2.119 1.833 2.386 2.534 1.225 2.614 2.200 2.427	2.023 1.783 2.379 2.492 1.219 2.550 2.171 2.271	2.095 1.814 2.307 2.348 1.220 2.629 2.170 2.388	2.285 1.947 2.409 2.669 1.266 2.648 2.200 2.252	0.642 1.886 0.274 0.907 0.441 0.785 1.546 0.576	0.109 0.081 0.086 0.030 0.099 0.187 0.002 0.086	94 90 100 98 99 96 97 90	98 96 90 99 101 97 97	111 123 101 107 107 102 100 89	5 111 -55 14 -30 -10 43 -36	-81 -94 -86 -95 -84 -79 -100 -90	3.74E-6 1.98E-5 2.13E-6 4.12E-6 2.60E-6 2.92E-6 7.61E-6 2.04E-6	1.14E-5 3.47E-5 4.43E-6 1.35E-5 6.02E-6 8.18E-6 2.01E-5 5.15E-6	4.37E-5 6.10E-5 9.24E-6 3.86E-5 2.32E-5 3.85E-5 4.48E-5 1.82E-5
Prostate Cancer PC-3 DU-145	0.477	1.586	1.599 1.446	1.621	1.699	0.425	0.117	101 103	103 104	110 100	-11 47	-76 -97	3.14E-6 8.67E-6	8.11E-6 2.11E-5	4.02E-5 4.70E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T T-47D MDA-MB-468	0.321 C 0.677 1.447 0.742 0.682	1.580 1.517 2.443 1.424 1.275	1.523 1.505 2.378 1.415 1.238	1.457 1.540 2.387 1.351 1.252	1.351 1.608 2.580 1.387 1.278	0.421 0.792 1.963 0.960 0.685	0.170 0.240 1.165 0.144 0.130	95 99 94 99 94	90 103 94 89 96	82 111 114 95 101	8 14 52 32 1	-47 -65 -19 -81 -81	2.69E-6 4.23E-6 1.06E-5 5.16E-6 3.20E-6	1.39E-5 1.49E-5 5.33E-5 1.92E-5 1.01E-5	> 1.00E-4 6.50E-5 > 1.00E-4 5.35E-5 4.16E-5

Developmental Ther	apeutics Program	NSC: D-782288 / 1	Conc: 1.00E-5 Molar	Test Date: Oct 20, 2014
One Dose Mea	an Graph	Experiment ID: 1410	OS79	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Perc	cent
Panel/Cell Line Leukemia HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H322M NCI-H322M NCI-H322M NCI-H460 NCI-H522 Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer SF-268 SF-295 SF-339 SNB-75 U251 Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-20 SK-MEL-28 SK-MEL-20 OVCAR-3 OVCAR-4 OVCAR	Growth Percent 52.13 25.08 9.64 19.92 20.00 87.92 101.03 80.36 121.10 93.28 85.53 112.79 97.11 23.99 107.68 95.09 35.52 72.77 78.89 63.38 43.47 92.40 101.39 100.82 92.05 104.54 64.85 19.88 101.39 100.82 92.05 104.54 64.85 19.88 101.39 100.82 92.05 104.54 64.85 19.88 101.33 113.60 82.21 86.86 123.11 66.50 91.53	Mean Growth	Percent - Growth Perc	
Mean Delta	78.37 68.73			
Range	113.47 150	100 50	0 -50	-100 -150

		Natio	onal (Cano	er Ir	nstitu In-	ıte D ∙Vitro	evelop Testir	mer ng R	ntal T esult	hera s	peutio	cs Progran	า	
NSC : D - 782	289 / 1				Exp	erimer	nt ID:1	412NS93	}			Test	Гуре : 08	Units : N	Iolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Dece	mber 01,	2014			QNS	:	MC :	
COMI : KCN-F	PGJ-23				Sta	in Rea	gent : S	RB Dual	Pass	Related	ł	SSPL	: 0ZAS		
						Lo	og10 Co	ncentration						-	
Panel/Cell Line	Time Zero	Ctrl	-8.0	Mear -7.0	n Optica -6.0	l Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.715 0.879 0.211 0.753 0.786 0.443	2.688 2.917 1.565 2.564 2.272 2.040	2.656 2.917 1.488 2.598 2.312 2.038	2.618 2.979 1.618 2.573 2.300 1.939	1.337 2.580 0.793 1.820 1.387 1.010	0.735 0.741 0.291 0.709 0.677 0.443	0.415 0.529 0.264 0.682 0.495 0.400	98 100 94 102 103 100	96 103 104 101 102 94	32 83 43 59 40 35	1 -16 -6 -14	-42 -40 4 -9 -37 -10	5.19E-7 2.17E-6 7.67E-7 1.37E-6 6.99E-7 5.63E-7	1.06E-5 6.94E-6 > 1.00E-4 8.11E-6 5.54E-6 1.00E-5	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-92 HOP-92 NCI-H226 NCI-H23 NCI-H322M NCI-H322M	Cancer 0.335 0.623 0.670 1.383 0.904 0.340 0.831 0.602	1.656 2.028 1.768 1.867 1.741 1.421 1.871 1.748	1.543 1.987 1.673 1.800 1.664 1.392 1.842 1.636	1.591 1.891 1.590 1.811 1.683 1.370 1.852 1.633	1.701 1.994 1.748 1.871 1.729 1.301 1.778 1.481	1.236 1.013 0.751 1.688 1.482 0.249 1.284 0.228	0.077 0.028 0.053 0.076 0.266 0.063 0.089 0.125	91 97 91 86 91 97 97 90	95 90 84 93 95 98 90	103 98 98 101 99 89 91 77	68 28 7 63 69 -27 44 -62	-77 -96 -92 -95 -71 -82 -89 -79	1.33E-5 4.80E-6 3.39E-6 1.21E-5 1.37E-5 2.17E-6 7.30E-6 1.56E-6	2.95E-5 1.68E-5 1.19E-5 2.51E-5 3.12E-5 5.86E-6 2.13E-5 3.57E-6	6.50E-5 4.27E-5 3.77E-5 5.22E-5 7.12E-5 2.64E-5 5.06E-5 8.18E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12	0.403 0.326 0.130 0.297 0.245 0.457	1.375 1.109 1.166 2.075 1.401 2.478	1.358 1.127 1.058 1.976 1.377 2.476	1.304 1.221 0.748 1.931 1.479 2.470	1.439 1.218 0.595 1.772 1.371 2.303	0.232 0.061 0.035 0.204 0.154 0.282	0.100 0.032 0.012 0.019 0.122 0.081	98 102 90 94 98 100	93 114 60 92 107 100	107 114 45 83 97 91	-43 -81 -73 -31 -37 -38	-75 -90 -91 -94 -50 -82	2.40E-6 2.12E-6 4.47E-7 1.94E-6 2.25E-6 2.08E-6	5.18E-6 3.83E-6 2.40E-6 5.31E-6 5.30E-6 5.06E-6	1.69E-5 6.91E-6 6.37E-6 1.99E-5 9.32E-5 1.84E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.497 0.877 1.078 0.428 0.762 0.335	1.849 3.041 2.975 1.528 1.669 1.675	1.822 2.885 2.914 1.499 1.551 1.639	1.748 2.835 2.827 1.495 1.504 1.650	1.681 3.043 2.952 1.450 1.643 1.532	0.628 0.697 1.311 0.532 1.340 0.335	0.140 0.058 0.237 0.102 0.316 0.035	98 93 97 97 87 97	93 90 92 97 82 98	88 100 99 93 97 89	10 -21 12 9 64	-72 -93 -78 -76 -59 -90	3.03E-6 2.60E-6 3.66E-6 3.27E-6 1.29E-5 2.75E-6	1.31E-5 6.76E-6 1.37E-5 1.29E-5 3.32E-5 9.96E-6	5.38E-5 2.54E-5 4.89E-5 4.93E-5 8.52E-5 3.61E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.206 0.764 0.409 0.484 1.232 0.966 1.000 0.576 0.537	1.437 1.381 1.700 2.531 2.293 2.731 3.146 1.482 1.972	1.367 1.351 1.733 2.527 2.223 2.694 3.103 1.409 1.894	1.316 1.370 1.623 2.383 2.214 2.653 3.121 1.460 1.935	0.613 1.365 1.552 2.206 2.140 2.743 3.108 1.429 1.827	0.033 0.731 0.442 0.277 1.033 0.719 0.036 0.481 0.292	0.022 0.180 0.128 0.017 0.234 0.134 0.033 0.069 0.135	94 95 103 100 93 98 98 92 95	90 98 94 93 93 96 99 98 97	33 97 88 84 86 101 98 94 90	-84 -4 3 -43 -16 -26 -96 -16 -46	-90 -76 -69 -97 -81 -86 -97 -88 -75	5.05E-7 2.93E-6 2.80E-6 1.86E-6 2.24E-6 2.52E-6 1.77E-6 2.51E-6 1.97E-6	1.91E-6 9.06E-6 1.08E-5 4.60E-6 6.94E-6 6.27E-6 3.20E-6 7.10E-6 4.60E-6	5.11E-6 4.30E-5 5.45E-5 3.32E-5 2.53E-5 5.78E-6 2.94E-5 1.40E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-4 OVCAR-8 NCI/ADR-RES SK-OV-3	0.586 0.448 0.692 0.609 0.431 0.338 0.700	2.081 1.686 1.466 1.513 1.846 1.419 1.602	2.118 1.701 1.473 1.539 1.834 1.399 1.700	2.145 1.721 1.395 1.544 1.864 1.402 1.548	2.086 1.640 1.455 1.695 1.820 1.304 1.661	0.779 0.457 0.933 0.756 0.627 0.379 1.064	0.280 0.023 0.068 0.152 0.148 0.271 0.006	102 101 103 99 98 111	104 103 91 103 101 98 94	100 96 99 120 98 89 107	13 1 31 16 14 40	-52 -95 -90 -75 -66 -20 -99	3.76E-6 3.05E-6 5.24E-6 4.73E-6 3.72E-6 2.88E-6 7.15E-6	1.58E-5 1.02E-5 1.80E-5 1.51E-5 1.49E-5 1.45E-5 1.95E-5	9.22E-5 3.39E-5 4.66E-5 5.32E-5 6.35E-5 > 1.00E-4 4.44E-5
Renal Cancer 786-0 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.598 0.522 0.527 0.601 0.536 0.763 0.666	2.244 2.299 2.824 1.262 1.707 2.072 2.555	2.210 2.324 2.735 1.245 1.647 2.021 2.451	2.109 2.316 2.617 1.257 1.769 2.006 2.447	2.236 2.448 2.803 1.292 1.764 2.064 2.475	0.467 0.230 0.451 0.166 0.496 1.004 0.436	0.056 0.086 -0.004 0.031 0.196 0.034 0.102	98 101 96 97 95 96 94	92 101 91 99 105 95 94	99 108 99 105 105 99 96	-22 -56 -15 -72 -7 18 -35	-91 -84 -100 -95 -64 -96 -85	2.55E-6 2.27E-6 2.70E-6 2.03E-6 3.08E-6 4.07E-6 2.24E-6	6.59E-6 4.57E-6 7.45E-6 3.90E-6 8.58E-6 1.45E-5 5.43E-6	2.56E-5 9.20E-6 2.60E-5 7.47E-6 5.74E-5 3.98E-5 2.03E-5
Prostate Cancer PC-3 DU-145	0.845 0.413	2.617 1.721	2.520 1.758	2.592 1.727	2.670 1.657	0.782 0.761	0.459 0.010	95 103	99 100	103 95	-7 27	-46 -98	3.02E-6 4.56E-6	8.56E-6 1.64E-5	> 1.00E-4 4.13E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 BT-549 T-47D MDA-MB-468	0.379 0.596 1.123 0.692 0.775	2.034 1.442 2.342 1.406 1.588	1.934 1.425 2.350 1.358 1.544	1.798 1.473 2.239 1.270 1.512	1.276 1.597 2.338 1.339 1.537	0.427 0.703 1.014 0.838 0.571	0.125 0.269 0.043 0.202 0.158	94 98 101 93 95	86 104 92 81 91	54 118 100 91 94	3 13 -10 20 -26	-67 -55 -96 -71 -80	1.21E-6 4.43E-6 2.84E-6 3.79E-6 2.31E-6	1.10E-5 1.54E-5 8.15E-6 1.67E-5 6.04E-6	5.69E-5 8.45E-5 2.92E-5 5.90E-5 2.78E-5

		Natio	onal	Cano	er Ir	nstitu In-	ite De Vitro	evelop Testir	men ng R	ital T esult	hera s	peutio	cs Program	l	
NSC : D - 782	137 / 1				Exp	erimer	nt ID:1	410NS77	,			Test	Type : 08	Units : N	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Octob	er 27, 20	14			QNS	:	MC :	
COMI : KCN-F	PGJ-11				Sta	in Rea	gent : S	RB Dual-	Pass I	Related	ł	SSPL	: 0ZAS		
						Lo	og10 Cor	centration	_			•		•	
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	n Optica -6.0	I Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.340 0.973 0.334 0.644 0.758 0.284	1.504 3.152 2.688 2.341 2.740 1.602	1.485 3.095 2.675 2.311 2.724 1.523	1.449 3.067 2.619 2.247 2.667 1.469	0.469 2.577 1.384 1.397 1.872 0.568	0.326 0.886 0.465 0.473 0.710 0.262	0.235 0.585 0.312 0.471 0.477 0.212	98 97 99 98 99 94	95 96 97 94 96 90	11 74 45 44 56 22	-4 -9 6 -27 -6 -8	-31 -40 -7 -27 -37 -25	3.45E-7 1.93E-6 7.89E-7 7.73E-7 1.26E-6 3.84E-7	5.27E-6 7.79E-6 2.83E-5 4.22E-6 7.90E-6 5.44E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H460 NCI-H522	Cancer 0.444 0.724 0.644 1.250 1.157 0.578 1.071 0.190 1.254	1.860 1.890 1.805 1.723 2.404 1.791 2.481 2.292 2.639	1.750 1.804 1.780 1.670 2.462 1.820 2.428 2.218 2.523	1.767 1.754 1.698 1.677 2.351 1.805 2.508 2.274 2.613	1.842 1.852 1.591 1.805 2.452 1.684 2.454 2.199 1.989	0.417 0.953 0.433 1.081 0.398 0.254 1.130 0.216 0.297	0.071 0.130 0.065 0.379 0.062 0.039 0.096 0.088	92 93 98 105 102 96 96 92	93 88 91 90 96 101 102 99 98	99 97 82 117 104 91 98 96 53	-6 20 -33 -14 -66 -56 4 1 -76	-84 -100 -80 -95 -67 -89 -96 -49 -93	2.91E-6 4.04E-6 3.27E-6 2.08E-6 3.26E-6 3.25E-6 3.04E-6 1.06E-6	8.73E-6 1.46E-5 5.16E-6 7.88E-6 4.10E-6 4.16E-6 1.10E-5 1.06E-5 2.57E-6	3.66E-5 3.82E-5 2.32E-5 2.81E-5 8.09E-6 9.10E-6 3.46E-5 > 1.00E-4 6.26E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.558 0.701 0.520 0.225 0.422 0.465 0.239	2.115 2.620 3.241 1.614 2.139 2.899 2.315	2.079 2.513 3.172 1.554 2.164 2.959 2.309	2.033 2.563 3.182 1.578 2.189 2.979 2.270	2.016 2.859 2.284 0.962 1.908 2.467 1.641	0.290 0.040 0.091 0.114 0.227 0.339 0.319	0.144 0.023 0.020 0.017 0.078 0.134 0.149	98 94 97 96 101 102 100	95 97 98 97 103 103 98	94 112 65 53 87 82 68	-48 -94 -83 -50 -46 -27 4	-74 -97 -96 -92 -82 -71 -38	2.03E-6 2.00E-6 1.26E-6 1.07E-6 1.89E-6 1.97E-6 1.89E-6	4.58E-6 3.50E-6 2.75E-6 3.29E-6 4.49E-6 5.65E-6 1.24E-5	1.19E-5 6.10E-6 6.02E-6 1.02E-5 1.28E-5 3.30E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.518 0.944 1.012 0.799 0.973 0.760	1.743 2.822 2.870 2.508 1.967 2.408	1.691 2.807 2.886 2.402 1.827 2.281	1.684 2.786 2.774 2.365 1.753 2.319	1.518 2.910 3.002 2.183 1.834 2.129	0.662 0.640 0.965 1.069 1.594 0.397	0.141 0.039 0.116 0.100 0.278 0.046	96 99 101 94 86 92	95 98 95 92 78 95	82 105 107 81 87 83	12 -32 -5 16 62 -48	-73 -96 -89 -88 -71 -94	2.84E-6 2.51E-6 3.24E-6 2.99E-6 1.24E-5 1.79E-6	1.38E-5 5.82E-6 9.09E-6 1.42E-5 2.93E-5 4.31E-6	5.38E-5 1.90E-5 3.47E-5 4.33E-5 6.91E-5 1.12E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.293 0.805 0.473 0.492 1.312 0.623 1.114 1.117 0.587	2.107 1.756 2.032 2.740 2.457 1.863 3.080 2.183 2.493	2.086 1.714 1.999 2.617 2.413 1.863 3.055 2.092 2.313	1.997 1.746 1.848 2.555 2.421 1.824 2.985 2.107 2.335	0.235 1.666 1.544 2.102 2.380 1.792 2.874 2.092 1.694	0.023 0.673 0.293 0.544 1.140 0.345 0.050 0.995 0.320	0.019 0.208 0.063 0.060 0.212 0.096 0.021 0.086 0.135	99 96 95 96 100 99 92 91	94 99 88 92 97 97 95 93 93	-20 91 69 72 93 94 90 92 58	-92 -16 -38 2 -13 -45 -96 -11 -45	-94 -74 -87 -88 -84 -85 -98 -92 -77	2.43E-7 2.39E-6 1.50E-6 2.05E-6 2.55E-6 2.08E-6 2.54E-6 1.64E-6 1.20E-6	6.68E-7 7.03E-6 1.06E-5 7.53E-6 4.77E-6 3.05E-6 7.82E-6 3.64E-6	2.60E-6 3.82E-5 1.75E-5 3.81E-5 3.32E-5 1.36E-5 5.68E-6 3.02E-5 1.39E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.881 0.472 0.677 0.725 0.604 0.586 0.850	2.515 1.801 1.654 2.138 2.360 1.961 1.659	2.543 1.841 1.640 2.188 2.369 1.990 1.671	2.614 1.808 1.585 2.073 2.313 2.009 1.589	2.527 1.320 1.572 2.270 2.172 1.727 1.778	0.761 0.218 0.997 0.713 0.841 0.544 1.075	0.198 0.016 0.077 0.251 0.047 0.218 0.004	102 103 98 104 100 102 102	106 101 93 95 97 103 91	101 64 92 109 89 83 115	-14 -54 33 -2 13 -7 28	-78 -97 -89 -65 -92 -63 -100	2.78E-6 1.31E-6 5.09E-6 3.42E-6 3.30E-6 2.32E-6 5.55E-6	7.60E-6 3.49E-6 1.86E-5 9.65E-6 1.34E-5 8.33E-6 1.65E-5	3.71E-5 9.28E-6 4.81E-5 5.73E-5 3.99E-5 5.87E-5 4.08E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.788 1.169 0.537 0.594 1.270 0.664 0.886 0.987	2.809 1.977 2.261 2.779 1.824 2.589 1.957 2.642	2.727 2.020 2.230 2.690 1.789 2.518 1.889 2.393	2.673 1.740 2.179 2.522 1.761 2.538 1.883 2.523	2.747 2.167 2.206 2.699 1.854 2.459 1.935 2.459	0.170 0.425 0.188 1.037 0.231 0.570 0.923 0.199	0.005 0.049 0.042 0.012 0.061 0.189 0.008 0.038	96 105 98 96 94 96 94 85	93 71 95 88 89 97 93 93	97 123 97 96 105 93 98 89	-78 -64 -65 20 -82 -14 3 -80	-99 -96 -92 -98 -95 -72 -99 -96	1.85E-6 2.47E-6 1.95E-6 4.07E-6 2.53E-6 3.22E-6 1.70E-6	3.57E-6 4.57E-6 3.97E-6 1.48E-5 3.66E-6 7.38E-6 1.08E-5 3.36E-6	6.88E-6 8.45E-6 8.08E-6 3.93E-5 6.76E-6 4.21E-5 3.32E-5 6.66E-6
Prostate Cancer PC-3 DU-145	0.736 0.413	1.762 1.586	1.727 1.607	1.762 1.608	1.794 1.509	0.617 0.646	0.152 0.005	97 102	100 102	103 93	-16 20	-79 -99	2.79E-6 3.89E-6	7.31E-6 1.47E-5	3.42E-5 3.88E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.396 C 0.568 0.973 1.343 0.680 0.703	2.208 1.400 1.952 2.813 1.407 1.356	2.109 1.393 1.865 2.787 1.392 1.359	1.898 1.430 1.893 2.689 1.319 1.316	0.897 1.400 1.979 2.673 1.275 1.264	0.407 0.483 1.437 0.893 0.799 0.259	0.190 0.114 0.890 0.012 0.269 0.115	94 99 91 98 98 100	83 104 94 92 88 94	28 100 103 91 82 86	1 -15 47 -34 16 -63	-52 -80 -9 -99 -61 -84	3.93E-7 2.72E-6 8.98E-6 2.12E-6 3.06E-6 1.74E-6	1.03E-5 7.41E-6 7.03E-5 5.37E-6 1.63E-5 3.77E-6	9.11E-5 3.46E-5 > 1.00E-4 1.78E-5 7.30E-5 8.16E-6

		Nati	onal	Cano	er Ir	nstitu In-	ıte D ∙Vitro	evelop Testii	omer ng R	ital T esult	hera s	peutio	cs Prograr	n	
NSC : D - 786	056 / 1				Exp	erimer	nt ID : 1	509NS56	6			Test	Гуре : 08	Units : M	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Septe	ember 08,	2015			QNS	:	MC :	
COMI : KCN-F	PGJ-56				Sta	in Rea	gent : S	SRB Dual	-Pass I	Related	ł	SSPL	: 0ZAS		
					0-1	Lo	og10 Cor	ncentration							
Panel/Cell Line	Zero	Ctrl	-8.8	Mear -7.8	-6.8	-5.8	es -4.8	-8.8	-7.8	ercent G -6.8	-5.8	-4.8	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.854 0.734 0.259 0.951 0.482 0.285	3.376 3.158 2.594 3.374 1.873 0.876	3.370 3.165 2.631 3.348 1.894 0.882	3.291 3.128 2.628 3.367 1.810 0.873	3.121 2.979 2.455 3.307 1.483 0.772	0.859 0.789 0.310 1.821 0.341 0.288	0.720 0.663 0.236 0.770 0.303 0.257	100 100 102 99 101 101	97 99 101 100 95 99	90 93 94 97 72 82	2 2 36 -29	-16 -10 -9 -19 -37 -10	4.65E-7 4.95E-7 5.03E-7 9.84E-7 2.75E-7 4.15E-7	1.71E-6 2.58E-6 2.60E-6 7.51E-6 8.58E-7 1.84E-6	> 1.67E-5 > 1.67E-5 > 1.67E-5 > 1.67E-5 > 1.67E-5 > 1.67E-5 > 1.67E-5
Non-Small Cell Lung A549/ATCC EKVX HOP-82 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.397 0.829 0.551 1.496 0.568 0.617 0.662 0.217 0.922	2.075 2.143 1.569 1.954 1.526 1.833 1.886 2.453 2.327	2.056 2.123 1.543 1.883 1.480 1.785 1.845 2.503 2.188	2.085 2.109 1.581 1.873 1.474 1.797 1.853 2.541 2.149	1.939 2.109 1.489 1.846 1.455 1.698 1.801 2.365 2.034	0.533 1.254 0.286 1.749 0.420 0.937 1.069 0.233 0.214	0.220 0.235 0.180 0.592 0.109 0.305 0.094 0.117 0.108	99 98 97 84 95 96 97 102 90	101 97 101 82 95 97 97 104 87	92 97 92 76 93 89 93 96 79	8 32 -48 55 -26 26 33 1 -77	-45 -72 -67 -60 -81 -51 -86 -46 -88	5.28E-7 8.93E-7 3.33E-7 1.85E-6 3.82E-7 6.98E-7 8.77E-7 5.08E-7 2.57E-7	2.38E-6 3.42E-6 7.57E-7 5.01E-6 1.01E-6 3.67E-6 3.18E-6 1.73E-6 5.37E-7	> 1.67E-5 1.03E-5 2.08E-6 1.36E-5 4.56E-6 1.64E-5 8.35E-6 > 1.67E-5 1.12E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.482 0.664 0.329 0.237 0.374 0.429 0.230	1.456 2.308 2.673 1.473 1.962 2.530 2.012	1.493 2.341 2.778 1.443 2.002 2.369 1.981	1.521 2.419 2.646 1.452 2.043 2.551 1.971	1.535 2.542 2.574 1.245 2.036 2.290 1.876	0.187 0.242 0.087 0.160 0.134 0.154 0.314	0.062 0.101 0.023 0.109 0.061 0.062 0.118	104 102 104 98 103 92 98	107 107 99 98 105 101 98	108 114 96 82 105 89 92	-61 -64 -74 -32 -64 -64 5	-87 -85 -93 -54 -84 -86 -49	3.68E-7 3.84E-7 3.11E-7 3.16E-7 3.52E-7 2.99E-7 5.08E-7	7.27E-7 7.33E-7 6.14E-7 8.67E-7 6.96E-7 6.35E-7 2.05E-6	1.43E-6 1.40E-6 1.21E-6 1.09E-5 1.38E-6 1.35E-6 > 1.67E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.431 0.834 0.954 0.499 0.861 0.301	1.676 2.654 2.682 1.753 1.552 1.499	1.689 2.556 2.582 1.722 1.456 1.472	1.690 2.617 2.671 1.702 1.468 1.436	1.542 2.513 2.645 1.688 1.377 1.283	0.555 0.676 1.284 0.902 1.128 0.324	0.058 0.209 0.451 0.197 0.026 0.020	101 95 94 98 86 98	101 98 99 96 88 95	89 92 98 95 75 82	10 -19 19 32 39 2	-87 -75 -53 -61 -97 -94	5.22E-7 4.01E-7 6.76E-7 8.67E-7 8.06E-7 4.19E-7	2.12E-6 1.13E-6 3.08E-6 3.71E-6 3.22E-6 1.75E-6	6.98E-6 5.98E-6 1.53E-5 1.29E-5 7.52E-6 5.84E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-5 UACC-62	0.426 0.729 0.602 0.472 0.964 0.780 0.839 0.703	2.682 1.323 2.494 2.340 1.730 2.168 2.947 2.419	2.670 1.310 2.461 2.288 1.746 2.241 2.941 2.207	2.617 1.284 2.475 2.309 1.754 2.231 2.919 2.204	2.413 1.335 2.380 2.208 1.599 2.102 2.809 2.001	0.118 0.769 0.612 0.439 0.828 0.926 0.452 0.430	0.051 0.425 0.254 0.125 0.133 0.230 0.051 0.329	99 98 97 102 105 100 88	97 94 99 103 105 99 87	88 102 94 93 83 95 93 76	-72 7 -7 -14 10 -46 -39	-88 -42 -58 -74 -86 -71 -94 -53	2.88E-7 5.87E-7 4.93E-7 4.49E-7 3.64E-7 5.71E-7 3.42E-7 2.80E-7	5.91E-7 2.29E-6 1.70E-6 1.42E-6 1.19E-6 2.25E-6 7.80E-7 7.65E-7	1.21E-6 > 1.67E-5 1.23E-5 7.38E-6 5.25E-6 9.32E-6 2.01E-6 9.91E-6
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.829 0.442 0.661 0.754 0.496 0.560 0.802	2.155 1.630 1.333 2.075 2.102 1.868 1.490	2.194 1.741 1.339 2.039 2.103 1.881 1.490	2.164 1.625 1.304 2.038 2.119 1.880 1.495	2.248 1.626 1.231 2.080 1.947 1.788 1.550	0.880 0.464 0.793 0.977 0.448 0.788 0.935	0.434 0.039 0.054 0.409 0.388 0.606 0.355	103 109 101 97 100 101 100	101 100 96 97 101 101 101	107 100 85 100 90 94 109	4 20 17 -10 17 19	-48 -91 -92 -46 -22 4 -56	5.96E-7 5.37E-7 5.71E-7 6.70E-7 4.23E-7 6.27E-7 7.57E-7	1.98E-6 1.75E-6 2.50E-6 3.11E-6 1.34E-6 > 1.67E-5 3.02E-6	> 1.67E-5 6.02E-6 7.03E-6 > 1.67E-5 > 1.67E-5 > 1.67E-5 1.40E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.605 1.169 0.483 0.592 0.963 0.648 0.762 0.811	2.452 2.063 1.990 2.147 1.620 2.117 1.623 2.173	2.299 2.049 2.014 1.996 1.614 1.956 1.532 2.026	2.305 1.984 2.006 1.999 1.608 2.032 1.549 1.982	2.266 2.023 2.054 2.005 1.548 1.989 1.635 2.023	0.255 1.911 0.112 0.522 0.893 0.696 0.857 0.273	0.022 0.062 0.090 0.126 0.142 0.428 0.114 0.029	92 98 102 90 99 89 89 89	92 91 101 90 98 94 91 86	90 96 104 91 89 91 101 89	-58 83 -77 -12 -7 3 11 -66	-96 -95 -81 -79 -85 -34 -85 -96	3.11E-7 2.56E-6 3.33E-7 4.17E-7 4.24E-7 4.92E-7 6.18E-7 2.98E-7	6.78E-7 4.89E-6 6.29E-7 1.28E-6 1.40E-6 2.04E-6 2.17E-6 6.24E-7	1.48E-6 9.35E-6 1.19E-6 6.21E-6 5.89E-6 > 1.67E-5 7.21E-6 1.31E-6
Prostate Cancer PC-3 DU-145 Broast Concer	0.649 0.284	2.593 1.440	2.547 1.469	2.512 1.477	2.433 1.352	0.919 0.477	0.309 0.005	98 103	96 103	92 92	14 17	-52 -98	5.74E-7 6.07E-7	2.71E-6 2.33E-6	1.54E-5 6.35E-6
MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.405 C 0.619 1.054 1.183 0.750 0.794	2.299 1.725 2.140 2.225 1.532 1.666	2.101 1.698 2.078 2.102 1.495 1.656	2.159 1.670 2.153 2.128 1.490 1.615	1.630 1.737 2.159 2.060 1.452 1.538	0.714 0.849 1.496 0.508 0.917 0.915	0.232 0.504 0.921 0.209 0.228 0.284	90 97 94 88 95 99	93 95 101 91 95 94	65 101 102 84 90 85	16 21 41 -57 21 14	-43 -19 -13 -82 -70 -64	3.36E-7 7.22E-7 1.17E-6 2.92E-7 6.35E-7 5.21E-7	3.16E-6 5.63E-6 9.68E-6 6.59E-7 2.86E-6 2.51E-6	> 1.67E-5 > 1.67E-5 > 1.67E-5 1.67E-5 1.49E-6 1.02E-5 1.10E-5

		Natio	onal	Cano	er Ir	nstitu In-	ute D -Vitro	evelop Testi	omer ng R	ntal T esult	hera s	peuti	cs Progran	n	
NSC : D - 788	3110 / 1				Exp	erimer	nt ID : 1	512NS26	6			Test	Type : 08	Units : N	Iolar
Report Date :	Februa	ry 08, 20)16		Tes	t Date	: Dece	mber 20,	2015			QNS	:	MC :	
COMI : KCN-I	PGJ-13				Sta	in Rea	gent : S	SRB Dual	-Pass I	Related	I	SSPL	: 0ZAS		
						L	og10 Co	ncentration						•	
Panel/Cell Line	Time Zero	Ctrl	-8.3	Mear -7.3	o Optica -6.3	I Densiti -5.3	ies -4.3	-8.3	P -7.3	ercent G -6.3	Fowth -5.3	-4.3	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.564 1.034 0.258 0.567 0.864 0.327	2.319 2.828 1.876 2.321 2.322 1.678	2.213 2.644 1.888 2.308 2.328 1.682	2.138 2.769 1.917 2.219 2.255 1.593	1.379 2.726 1.444 1.643 1.728 0.801	0.591 0.917 0.379 0.615 0.701 0.374	0.411 0.818 0.347 0.484 0.476 0.326	94 90 101 99 100 100	90 97 103 94 95 94	46 94 73 61 59 35	2 -11 7 3 -19 3	-27 -21 6 -15 -45	4.13E-7 1.31E-6 1.13E-6 7.80E-7 6.57E-7 2.78E-7	5.66E-6 3.91E-6 > 5.00E-5 7.17E-6 2.86E-6 3.82E-5	<pre>> 5.00E-5 > 5.00E-5</pre>
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.329 0.709 0.869 1.598 1.106 0.631 0.715 0.243 1.165	1.311 2.107 1.861 2.022 2.703 2.033 2.070 2.587 1.859	1.185 2.090 1.824 1.952 2.567 1.960 1.907 2.718 1.778	1.223 1.972 1.850 1.917 2.527 1.930 1.943 2.601 1.771	1.293 2.050 1.897 2.458 1.835 2.012 2.541 1.625	0.355 0.877 0.825 1.622 0.428 0.445 1.275 0.202 0.472	0.136 0.346 0.153 0.336 0.104 0.156 0.058 0.126 0.142	87 99 96 83 91 95 88 106 88	91 90 95 89 93 91 101 87	98 96 104 92 85 86 96 98 66	3 -5 -61 -29 41 -17 -60	-59 -51 -82 -79 -91 -75 -92 -48 -88	1.60E-6 1.76E-6 1.52E-6 8.63E-7 1.02E-6 3.46E-6 1.31E-6 6.73E-7	5.52E-6 7.73E-6 4.49E-6 5.81E-6 1.90E-6 2.78E-6 1.02E-5 3.55E-6 1.68E-6	3.61E-5 4.77E-5 1.90E-5 2.27E-5 4.18E-6 1.40E-5 2.42E-5 > 5.00E-5 4.20E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 SW-620	0.450 0.764 0.315 0.356 0.281 0.245	1.409 2.427 2.155 2.183 1.178 1.655	1.436 2.404 2.122 2.153 1.161 1.673	1.423 2.567 2.008 2.113 1.174 1.718	1.359 2.713 0.859 1.798 1.067 1.603	0.313 0.112 0.136 0.369 0.172 0.242	0.103 0.041 0.007 0.036 0.123 0.127	103 99 98 98 98 101	101 108 92 96 99 104	95 117 30 79 88 96	-30 -85 -57 1 -39 -1	-77 -95 -98 -90 -56 -48	1.14E-6 1.07E-6 2.35E-7 1.17E-6 9.91E-7 1.49E-6	2.86E-6 1.89E-6 1.10E-6 5.09E-6 2.46E-6 4.83E-6	1.31E-5 3.34E-6 4.17E-6 1.81E-5 2.15E-5 > 5.00E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.589 0.799 1.079 0.772 0.954 0.346	2.094 2.666 2.747 2.563 1.711 1.249	2.031 2.647 2.725 2.499 1.542 1.207	1.979 2.585 2.677 2.395 1.505 1.184	1.899 2.704 2.670 2.469 1.482 0.939	0.990 0.595 0.939 1.489 1.338 0.194	0.156 0.043 0.038 0.102 0.308 0.008	96 99 99 96 78 95	92 96 91 73 93	87 102 95 95 70 66	27 -26 -13 40 51 -44	-74 -95 -96 -87 -68 -98	2.05E-6 1.28E-6 3.29E-6 5.07E-6 6.95E-7	9.22E-6 3.15E-6 3.79E-6 1.03E-5 1.34E-5 1.99E-6	2.91E-5 1.13E-5 1.39E-5 2.56E-5 3.54E-5 6.48E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.493 0.845 0.628 0.598 0.820 0.705 0.812 0.963 0.761	2.946 1.845 2.047 2.869 1.145 1.856 2.898 1.736 2.738	2.817 1.768 2.026 2.960 1.157 1.815 2.807 1.556 2.645	2.791 1.751 1.878 3.564 1.149 1.799 2.846 1.484 2.600	2.429 1.765 1.845 2.634 1.092 1.716 2.551 1.549 2.481	0.084 1.036 0.641 0.748 0.582 0.563 0.033 0.630 0.542	0.025 0.294 0.091 0.099 0.208 0.167 0.014 0.044 0.192	95 92 99 104 104 96 96 77 95	94 91 88 131 101 95 97 67 93	79 92 86 90 84 88 83 76 87	-83 19 1 -29 -20 -96 -35 -29	-95 -65 -86 -83 -75 -76 -98 -95 -75	7.54E-7 1.88E-6 1.32E-6 1.50E-6 9.95E-7 1.12E-6 7.67E-7 8.56E-7 1.04E-6	1.54E-6 8.42E-6 5.92E-6 2.76E-6 3.25E-6 1.46E-6 2.43E-6 2.82E-6	3.13E-6 3.30E-5 1.94E-5 2.13E-5 1.44E-5 1.70E-5 2.77E-6 8.94E-6 1.45E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.722 0.409 0.700 0.583 0.540 0.584 0.677	2.307 1.422 1.658 1.651 1.701 2.074 1.260	2.331 1.435 1.628 1.622 1.680 2.089 1.221	2.356 1.450 1.566 1.593 1.609 2.043 1.214	2.251 1.319 1.553 1.598 1.513 1.915 1.271	0.997 0.499 0.980 0.739 0.530 0.479 0.897	0.205 0.028 0.043 0.237 0.205 0.396 0.115	102 101 97 98 101 93	103 103 90 95 92 98 92	96 90 89 95 84 89 102	17 9 29 15 -2 -18 38	-72 -93 -94 -59 -62 -32 -83	1.93E-6 1.55E-6 2.25E-6 1.81E-6 1.24E-6 1.16E-6 3.21E-6	7.84E-6 6.11E-6 8.64E-6 7.88E-6 4.76E-6 3.40E-6 1.02E-5	2.86E-5 1.89E-5 2.20E-5 3.74E-5 3.15E-5 > 5.00E-5 2.66E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.761 1.358 0.480 0.655 0.996 0.940 0.937 0.913	2.253 2.468 1.768 3.058 1.789 3.095 1.406 2.318	2.155 2.304 1.802 3.042 1.734 3.101 1.359 2.181	2.144 2.241 1.761 3.637 1.707 3.114 1.378 2.138	2.354 2.560 1.652 2.994 1.732 3.001 1.493 2.205	0.456 2.161 0.209 0.634 0.127 1.211 0.814 0.141	0.013 0.096 0.143 -0.004 0.057 0.497 0.110 0.048	93 85 103 99 93 100 90 90	93 80 99 124 90 101 94 87	107 108 91 97 93 96 119 92	-40 72 -57 -3 -87 13 -13 -85	-98 -93 -70 -100 -94 -47 -88 -95	1.22E-6 6.83E-6 9.47E-7 1.48E-6 8.65E-7 1.77E-6 1.66E-6 8.64E-7	2.67E-6 1.37E-5 2.07E-6 4.65E-6 1.64E-6 8.12E-6 3.97E-6 1.66E-6	7.39E-6 2.75E-5 4.51E-6 1.52E-5 3.10E-6 > 5.00E-5 1.55E-5 3.19E-6
Prostate Cancer PC-3 DU-145	0.785 0.321	1.981 1.648	1.891 1.657	1.978 1.621	1.872 1.496	0.797 0.554	0.423 0.030	92 101	100 98	91 89	1 18	-46 -91	1.43E-6 1.75E-6	5.25E-6 7.26E-6	> 5.00E-5 2.10E-5
Breast Cancer MCF7 MDA-MB-231/ATC HS 578T BT-549 MDA-MB-468	0.510 C 0.664 1.143 1.144 1.213	2.682 1.738 2.405 2.238 2.404	2.614 1.748 2.318 2.255 2.310	2.408 1.698 2.235 2.157 2.277	1.359 1.725 2.468 2.225 2.265	0.710 0.837 1.726 0.832 1.095	0.238 0.214 1.127 0.089 0.223	97 101 93 101 92	87 96 87 93 89	39 99 105 99 88	9 16 46 -27 -10	-53 -68 -1 -92 -82	2.97E-7 1.95E-6 4.30E-6 1.22E-6 1.23E-6	7.01E-6 7.78E-6 4.66E-5 3.04E-6 3.98E-6	4.41E-5 3.07E-5 > 5.00E-5 1.12E-5 1.81E-5

		Natio	onal	Cano	er Ir	nstitu In-	ıte D ∙Vitro	evelop Testir	men ng R	ital T esult	hera s	peuti	cs Program	l	
NSC : D - 786	057 / 1				Exp	erimer	nt ID:1	509NS56	6			Test	Туре : 08	Units : N	lolar
Report Date :	Decemb	ber 27, 2	2015		Tes	t Date	: Septe	ember 08,	2015			QNS	:	MC :	
COMI : KCN-F	PGJ-57				Sta	in Rea	gent : S	RB Dual	Pass I	Related	1	SSPL	: 0ZAS		
	_					Lo	og10 Cor	ncentration							
Panel/Cell Line	Zero	Ctrl	-8.3	Mear -7.3	-6.3	-5.3	es -4.3	-8.3	-7.3	ercent G -6.3	-5.3	-4.3	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.854 0.734 0.259 0.951 0.482 0.285	3.376 3.015 2.439 3.169 1.883 0.843	3.354 2.956 2.363 3.153 1.878 0.847	3.325 2.861 2.278 3.178 1.883 0.810	2.429 2.508 1.509 2.931 0.920 0.509	0.854 0.690 0.251 0.856 0.369 0.277	0.650 0.608 0.232 0.636 0.331 0.254	99 97 97 99 100 101	98 93 100 100 94	62 78 57 89 31 40	-6 -3 -10 -24 -3	-24 -17 -33 -31 -11	7.91E-7 1.07E-6 6.61E-7 1.24E-6 2.67E-7 3.28E-7	5.00E-6 4.23E-6 4.44E-6 3.96E-6 1.86E-6 4.26E-6	> 5.00E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	Cancer 0.397 0.829 0.551 1.496 0.568 0.617 0.662 0.217 0.922	1.903 1.975 1.520 2.067 1.608 1.881 1.881 2.399 2.498	1.884 1.983 1.557 1.993 1.556 1.837 1.828 2.443 2.427	1.837 1.965 1.547 1.987 1.511 1.800 1.781 2.464 2.395	1.735 1.953 1.336 2.126 1.432 1.667 1.649 2.086 1.930	0.361 1.002 0.450 1.540 0.585 0.287 0.897 0.188 0.464	0.108 0.224 0.165 0.485 0.150 0.214 0.058 0.105 0.194	99 101 104 87 95 96 96 102 95	96 99 103 86 91 94 92 103 93	89 98 81 110 83 83 81 86 64	-9 -18 2 -53 19 -14 -50	-73 -73 -70 -68 -74 -65 -91 -52 -79	1.24E-6 1.90E-6 1.92E-6 1.27E-6 8.73E-7 1.59E-6 1.14E-6 6.63E-7	4.03E-6 7.42E-6 3.26E-6 6.33E-6 5.26E-6 2.03E-6 7.47E-6 3.65E-6 1.83E-6	2.19E-5 2.74E-5 2.04E-5 2.92E-5 2.43E-5 4.71E-6 2.12E-5 4.47E-5 5.13E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.482 0.664 0.329 0.237 0.374 0.429 0.230	1.501 2.346 2.952 1.312 2.244 2.311 1.846	1.545 2.334 2.907 1.302 2.156 2.341 1.861	1.527 2.366 2.983 1.268 2.243 2.306 1.913	1.418 2.469 1.547 0.910 1.861 1.900 1.147	0.214 0.096 0.269 0.151 0.234 0.238 0.219	0.077 0.079 0.052 0.033 0.152 0.117 0.128	104 99 98 99 95 102 101	103 101 101 96 100 100 104	92 107 46 63 79 78 57	-56 -86 -18 -36 -37 -45 -5	-84 -88 -84 -86 -59 -73 -45	9.61E-7 9.91E-7 6.70E-7 8.94E-7 8.48E-7 6.42E-7	2.10E-6 1.80E-6 2.61E-6 2.14E-6 2.39E-6 2.16E-6 4.15E-6	4.58E-6 3.27E-6 1.51E-5 9.34E-6 1.86E-5 7.76E-6 > 5.00E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.431 0.834 0.954 0.499 0.861 0.301	1.572 2.582 2.632 1.742 1.546 1.403	1.559 2.529 2.611 1.682 1.439 1.366	1.522 2.567 2.599 1.648 1.424 1.378	1.391 2.529 2.624 1.516 1.354 1.017	0.416 0.783 1.212 0.675 1.195 0.197	0.160 0.171 0.311 0.092 0.025 0.033	99 97 99 95 84 97	96 99 98 92 82 98	84 97 99 82 72 65	-4 -6 15 14 49 -35	-63 -79 -67 -82 -97 -89	1.23E-6 1.43E-6 1.94E-6 1.48E-6 4.38E-6 7.06E-7	4.55E-6 4.36E-6 7.67E-6 7.02E-6 1.08E-5 2.24E-6	3.02E-5 1.98E-5 3.08E-5 2.34E-5 2.37E-5 9.54E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-62	0.426 0.729 0.602 0.472 0.964 0.780 0.839 0.703	2.709 1.331 2.668 2.361 1.761 2.150 3.003 2.334	2.619 1.291 2.615 2.296 1.791 2.182 3.035 2.151	2.519 1.261 2.530 2.295 1.788 2.151 2.964 2.128	2.065 1.262 2.333 1.666 1.673 1.958 2.755 1.596	0.090 0.580 0.848 0.304 0.810 0.692 0.190 0.397	0.045 0.300 0.370 0.064 0.261 0.181 0.076 0.192	96 93 97 104 102 101 89	92 88 93 97 103 100 98 87	72 88 84 63 89 86 89 55	-79 -21 12 -36 -16 -11 -77 -44	-90 -59 -39 -87 -73 -73 -77 -91 -73	6.98E-7 1.13E-6 1.48E-6 6.80E-7 1.17E-6 8.54E-7 5.59E-7	1.50E-6 3.24E-6 8.61E-6 2.18E-6 3.52E-6 3.83E-6 1.71E-6 1.80E-6	3.21E-6 2.93E-5 5.00E-5 9.59E-6 1.97E-5 1.95E-5 3.42E-6 8.34E-6
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.829 0.442 0.661 0.754 0.496 0.560 0.802	2.105 1.492 1.310 2.016 2.049 1.875 1.417	2.142 1.500 1.332 1.959 2.033 1.913 1.436	2.150 1.543 1.311 1.944 1.993 1.835 1.492	2.102 1.005 1.144 2.008 1.419 1.457 1.481	0.774 0.391 0.811 0.855 0.667 0.669 0.930	0.318 0.021 0.054 0.387 0.361 0.520 0.090	103 101 103 95 99 103 103	104 105 100 94 96 97 112	100 54 74 99 59 68 110	-7 -12 23 8 11 8 21	-62 -95 -92 -49 -27 -7 -89	1.47E-6 5.68E-7 1.50E-6 1.74E-6 7.83E-7 1.01E-6 2.36E-6	4.33E-6 3.31E-6 7.94E-6 6.92E-6 9.71E-6 1.72E-5 7.74E-6	3.07E-5 1.44E-5 2.16E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5 2.21E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.605 1.169 0.483 0.592 0.963 0.648 0.762 0.811	2.430 1.996 1.934 2.180 1.648 2.015 1.557 2.146	2.376 2.003 1.966 2.030 1.715 1.998 1.518 1.991	2.402 1.898 2.022 2.096 1.662 1.963 1.578 1.953	2.359 1.963 1.638 2.000 1.604 1.744 1.672 1.813	0.332 0.683 0.091 0.275 0.347 0.471 0.728 0.185	0.111 0.050 0.070 0.020 0.098 0.366 0.152 0.151	97 101 102 91 110 99 95 88	98 88 106 95 102 96 103 86	96 96 80 94 80 114 75	-45 -42 -81 -54 -64 -27 -4 -77	-82 -96 -86 -97 -90 -44 -80 -81	1.06E-6 1.08E-6 7.63E-7 9.35E-7 9.45E-7 9.54E-7 1.74E-6 7.30E-7	2.40E-6 2.49E-6 1.56E-6 2.10E-6 1.96E-6 2.78E-6 4.59E-6 1.56E-6	6.79E-6 7.15E-6 3.20E-6 4.71E-6 4.07E-6 > 5.00E-5 2.00E-5 3.31E-6
Prostate Cancer PC-3 DU-145	0.649 0.284	2.652 1.342	2.661 1.393	2.658 1.342	2.336 1.144	0.748 0.391	0.297 0.015	100 105	100 100	84 81	5 10	-54 -95	1.35E-6 1.37E-6	6.05E-6 6.24E-6	4.24E-5 1.87E-5
MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.405 0.619 1.054 1.183 0.750 0.794	2.112 1.648 2.041 2.284 1.481 1.760	2.024 1.609 2.021 2.274 1.454 1.730	1.971 1.593 1.977 2.290 1.447 1.693	0.801 1.620 1.992 2.137 1.270 1.449	0.487 0.765 1.244 0.951 0.912 0.809	0.128 0.381 0.826 0.401 0.382 0.497	95 96 98 99 96 97	92 95 94 101 95 93	23 97 95 87 71 68	5 14 19 -20 22 2	-68 -39 -22 -66 -49 -37	2.03E-7 1.85E-6 1.96E-6 1.11E-6 1.35E-6 9.28E-7	5.82E-6 9.28E-6 1.48E-5 3.27E-6 1.02E-5 5.46E-6	2.80E-5 > 5.00E-5 > 5.00E-5 2.25E-5 > 5.00E-5 > 5.00E-5

		Natio	onal	Cano	er Ir	nstitu In-	ite De Vitro	evelop Testir	mer ng R	ital T esult	hera s	peutio	cs Progran	n	
NSC : D - 783	636 / 1				Exp	erimer	nt ID:1	504NS69)			Test	Гуре : 08	Units : M	lolar
Report Date :	Decemb	ber 27, 2	2015		Tes	t Date	: April 1	13, 2015				QNS	:	MC :	
COMI : KCN-F	PGJ-42				Sta	in Rea	gent : S	RB Dual	Pass	Related	1	SSPL	: 0ZAS		
						Lo	og10 Cor	centration						•	
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	optica -6.0	I Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.574 1.047 0.333 0.964 0.812 0.493	2.169 3.076 2.111 3.064 2.974 1.675	2.201 3.037 2.086 3.041 3.037 1.636	2.123 3.056 2.103 3.120 3.069 1.606	0.997 2.881 1.700 2.708 2.299 0.938	0.593 0.866 0.336 0.840 0.850 0.463	0.385 0.724 0.211 0.571 0.661 0.289	102 98 99 99 103 97	97 99 100 103 104 94	27 90 77 83 69 38	1 -17 -13 2 -6	-33 -31 -37 -41 -19 -41	4.65E-7 2.37E-6 2.24E-6 2.21E-6 1.91E-6 6.04E-7	1.08E-5 6.90E-6 1.01E-5 7.34E-6 1.22E-5 7.22E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	Cancer 0.453 0.829 0.638 1.340 0.894 0.626 1.234 0.444 0.866	1.863 2.085 1.651 1.940 2.300 2.009 2.798 3.207 1.874	1.917 1.955 1.518 1.924 2.320 1.949 2.694 3.252 1.836	1.984 1.998 1.639 1.962 2.344 1.949 2.656 3.280 1.894	1.895 1.985 1.742 2.037 2.232 1.857 2.742 3.218 1.514	0.448 1.063 0.527 1.194 0.370 0.490 1.783 0.249 0.463	0.159 -0.007 0.118 0.161 0.621 0.164 0.093 0.245 0.302	104 90 87 97 101 96 93 102 96	109 93 99 104 103 96 91 103 102	102 92 109 116 95 89 96 100 64	-1 19 -17 -59 -22 35 -44 -47	-65 -100 -82 -88 -31 -74 -93 -45 -65	3.20E-6 3.73E-6 2.93E-6 3.32E-6 1.97E-6 2.25E-6 5.72E-6 2.23E-6 1.35E-6	9.76E-6 1.43E-5 7.27E-6 8.20E-6 4.16E-6 6.36E-6 1.88E-5 4.96E-6 3.80E-6	5.84E-5 3.79E-5 3.22E-5 3.21E-5 3.49E-5 4.64E-5 > 1.00E-4 1.54E-5
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.359 0.425 0.319 0.264 0.380 0.437 0.686	1.517 1.419 2.772 1.946 1.668 2.378 3.169	1.460 1.343 2.508 1.867 1.783 2.363 3.244	1.575 1.357 2.679 1.846 1.846 2.356 3.310	1.471 1.420 1.871 1.596 1.756 2.099 3.121	0.238 0.068 0.119 0.170 0.283 0.249 0.695	0.142 0.044 0.030 0.030 0.120 0.100 0.262	95 92 89 95 109 99 103	105 94 96 94 114 99 106	96 100 63 79 107 86 98	-34 -84 -63 -36 -26 -43	-60 -90 -91 -89 -68 -77 -62	2.26E-6 1.87E-6 1.27E-6 1.79E-6 2.69E-6 1.89E-6 3.10E-6	5.49E-6 3.50E-6 3.17E-6 4.88E-6 6.41E-6 4.62E-6 1.01E-5	4.05E-5 6.54E-6 7.91E-6 1.86E-5 3.72E-5 1.59E-5 6.44E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.763 0.867 1.112 0.565 0.683 0.592	2.312 2.599 2.965 2.098 1.594 2.143	2.257 2.540 2.738 2.104 1.461 2.184	2.229 2.585 2.908 2.138 1.518 2.196	2.122 2.621 2.885 1.944 1.492 1.796	0.971 0.626 0.875 0.327 1.129 0.197	0.396 0.119 0.082 0.132 0.052 0.015	96 97 88 100 85 103	95 99 97 103 92 103	88 101 96 90 89 78	13 -28 -21 -42 49 -67	-48 -86 -93 -77 -92 -97	3.22E-6 2.50E-6 2.46E-6 2.01E-6 9.41E-6 1.55E-6	1.65E-5 6.09E-6 6.57E-6 4.80E-6 2.22E-5 3.45E-6	> 1.00E-4 2.40E-5 2.52E-5 1.69E-5 5.01E-5 7.65E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.331 0.800 0.432 0.305 1.421 0.745 0.820 0.990 1.140	2.190 1.561 1.957 1.993 2.397 2.317 3.131 1.894 3.121	2.045 1.515 1.834 1.880 2.505 2.200 3.112 1.918 3.153	1.963 1.494 1.864 1.918 2.367 2.248 3.141 1.922 3.138	1.559 1.519 1.631 1.656 2.341 1.841 3.000 1.782 2.871	0.075 1.019 0.363 0.197 1.275 0.457 0.039 0.859 0.952	0.033 0.227 0.172 0.066 0.298 0.160 -0.002 0.175 0.270	92 94 93 111 93 99 103 102	88 91 96 97 96 100 103 101	66 95 79 80 94 70 94 88 87	-77 29 -16 -35 -10 -39 -95 -13 -16	-90 -72 -60 -79 -79 -79 -100 -82 -76	1.29E-6 4.75E-6 2.01E-6 1.82E-6 2.65E-6 1.52E-6 1.71E-6 2.36E-6 2.29E-6	2.89E-6 1.93E-5 6.76E-6 4.94E-6 7.98E-6 4.40E-6 3.14E-6 7.38E-6 6.94E-6	6.43E-6 6.08E-5 5.85E-5 2.18E-5 3.78E-5 1.92E-5 5.77E-6 3.40E-5 3.63E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.843 0.780 0.904 0.923 0.542 0.634 0.795	2.800 2.316 2.109 1.985 2.076 2.239 1.960	2.770 2.360 2.006 1.858 2.210 2.183 1.892	2.767 2.330 2.046 1.949 2.170 2.091 1.965	2.737 2.060 1.948 2.222 1.905 2.067 2.019	1.020 0.562 1.207 0.979 0.601 0.802 1.168	0.353 0.023 0.117 0.296 0.235 0.559 0.083	98 103 91 88 109 96 94	98 101 95 97 106 91 100	97 83 87 122 89 89 105	9 -28 25 5 4 10 32	-58 -97 -87 -68 -57 -12 -90	3.41E-6 1.99E-6 3.94E-6 4.15E-6 2.86E-6 3.15E-6 5.66E-6	1.36E-5 5.61E-6 1.68E-5 1.18E-5 1.16E-5 2.93E-5 1.83E-5	7.55E-5 2.08E-5 4.67E-5 5.69E-5 7.74E-5 > 1.00E-4 4.72E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.666 1.313 0.539 0.830 0.803 0.980 0.909 0.988	2.432 2.069 2.175 3.228 1.621 3.220 1.547 2.878	2.263 2.140 2.024 3.097 1.601 3.229 1.471 2.810	2.412 2.060 2.086 3.214 1.656 3.256 1.542 2.786	2.732 2.134 1.967 3.155 1.690 3.187 1.770 2.707	0.495 0.397 0.083 1.258 0.112 1.149 0.899 0.090	0.095 0.072 0.059 0.090 0.084 0.882 0.052 0.059	90 109 91 95 98 100 88 96	99 95 99 104 102 99 95	117 109 87 97 109 99 135 91	-26 -70 -85 18 -86 8 -1 -91	-86 -95 -89 -90 -10 -94 -94	2.95E-6 2.13E-6 1.65E-6 3.92E-6 2.00E-6 3.41E-6 4.21E-6 1.68E-6	6.61E-6 4.06E-6 3.22E-6 1.47E-5 3.61E-6 2.68E-5 9.82E-6 3.16E-6	2.54E-5 7.74E-6 6.28E-6 4.31E-5 6.53E-6 > 1.00E-4 3.35E-5 5.96E-6
Prostate Cancer PC-3 DU-145	0.571 0.326	2.301 1.546	2.280 1.545	2.381 1.486	2.269 1.308	0.584 0.342	0.259 0.030	99 100	105 95	98 80	1 1	-55 -91	3.12E-6 2.43E-6	1.03E-5 1.03E-5	8.24E-5 3.60E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.400 C 0.732 1.372 1.210 0.770 0.790	2.019 1.876 2.447 2.667 1.693 1.530	1.833 1.964 2.477 2.533 1.592 1.484	1.764 1.960 2.555 2.636 1.602 1.535	0.907 1.944 2.565 2.477 1.437 1.242	0.515 1.049 2.011 1.285 0.980 0.334	0.123 0.340 1.231 0.066 0.226 0.244	89 108 103 91 89 94	84 107 110 98 90 101	31 106 111 87 72 61	7 28 59 5 23 -58	-69 -54 -10 -95 -71 -69	4.44E-7 5.19E-6 1.37E-5 2.83E-6 2.82E-6 1.24E-6	1.24E-5 2.19E-5 7.12E-5 1.13E-5 1.75E-5 3.26E-6	5.60E-5 9.03E-5 > 1.00E-4 3.57E-5 6.00E-5 8.61E-6

		Natio	onal	Cano	er Ir	nstitu In-	ite De Vitro	evelop Testir	men ng R	ital T esult	hera s	peutio	s Progran	n	
NSC : D - 783	637 / 1				Exp	erimer	nt ID:1	504NS69)			Test	Гуре : 08	Units : N	lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: April 1	13, 2015				QNS	:	MC :	
COMI : KCN-F	PGJ-43				Sta	in Rea	gent : S	RB Dual	Pass I	Related	1	SSPL	: 0ZAS		
						Lo	og10 Cor	ncentration						•	
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	n Optica -6.0	I Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.574 1.047 0.333 0.964 0.812 0.493	2.135 3.034 2.172 3.153 3.052 1.707	2.262 3.215 2.264 3.136 3.102 1.582	2.237 3.077 2.266 3.141 3.162 1.590	1.383 2.928 1.831 2.935 2.794 1.095	0.611 0.880 0.304 0.761 0.896 0.409	0.418 0.622 0.222 0.661 0.637 0.319	108 109 105 99 102 90	106 102 105 99 105 90	52 95 81 90 88 50	2 -16 -9 -21 4 -17	-27 -41 -33 -31 -22 -35	1.09E-6 2.53E-6 2.23E-6 2.29E-6 2.85E-6 9.75E-7	1.20E-5 7.17E-6 7.98E-6 6.46E-6 1.40E-5 5.53E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	Cancer 0.453 0.829 0.638 1.340 0.894 0.626 1.234 0.444 0.866	1.966 2.155 1.722 1.960 2.312 2.014 2.760 3.246 1.884	2.024 1.950 1.593 1.952 2.257 1.905 2.585 3.323 1.830	1.988 2.018 1.697 1.975 2.334 1.892 2.638 3.336 1.826	1.983 2.062 1.820 2.024 2.246 1.847 2.700 3.235 1.728	0.577 1.192 0.610 1.176 0.353 0.406 1.714 0.294 0.617	0.064 -0.012 0.057 0.089 0.467 0.104 0.083 0.139 0.220	104 84 99 96 92 89 103 95	101 90 98 102 102 91 92 103 94	101 93 109 110 95 88 96 100 85	8 -4 -12 -61 -35 31 -34 -29	-86 -100 -91 -93 -48 -83 -93 -69 -75	3.55E-6 4.52E-6 3.32E-6 3.10E-6 1.95E-6 2.03E-6 5.17E-6 2.35E-6 2.02E-6	1.22E-5 1.64E-5 9.15E-6 7.94E-6 4.09E-6 5.18E-6 1.79E-5 5.57E-6 5.57E-6	4.16E-5 4.05E-5 3.36E-5 2.92E-5 4.50E-5 2.90E-5 2.90E-5 2.90E-5
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.359 0.425 0.319 0.264 0.380 0.437 0.686	1.579 1.406 2.861 1.994 1.824 2.390 3.280	1.509 1.381 2.685 1.852 1.871 2.425 3.338	1.578 1.432 2.849 1.899 1.896 2.347 3.361	1.566 1.402 2.497 1.617 1.946 2.198 3.316	0.251 0.043 0.138 0.266 0.202 0.731	0.124 0.029 0.027 0.009 0.114 0.059 0.242	94 97 93 92 103 102 102	100 103 100 95 105 98 103	99 100 86 78 108 90 101	-30 -90 -57 -48 -30 -54 2	-65 -93 -92 -97 -70 -87 -65	2.39E-6 1.83E-6 1.67E-6 2.64E-6 1.90E-6 3.28E-6	5.84E-6 3.35E-6 4.00E-6 4.18E-6 6.06E-6 4.23E-6 1.06E-5	3.66E-5 6.15E-6 8.97E-6 1.11E-5 3.14E-5 9.41E-6 6.00E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.763 0.867 1.112 0.565 0.683 0.592	2.344 2.775 2.909 2.142 1.574 2.225	2.280 2.501 2.743 2.115 1.437 2.238	2.232 2.675 2.807 2.172 1.476 2.206	2.236 2.617 2.838 2.012 1.444 2.082	0.843 0.553 1.074 0.927 1.016 0.356	0.112 0.058 0.067 0.105 0.017 0.006	96 86 91 98 85 101	93 95 94 102 89 99	93 92 96 92 85 91	5 -36 -3 23 37 -40	-85 -93 -94 -82 -98 -99	3.09E-6 2.12E-6 2.90E-6 4.04E-6 5.46E-6 2.06E-6	1.14E-5 5.21E-6 9.24E-6 1.66E-5 1.89E-5 4.96E-6	4.06E-5 1.74E-5 3.27E-5 4.99E-5 4.44E-5 1.48E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.331 0.800 0.432 0.305 1.421 0.745 0.820 0.990 1.140	2.315 1.593 2.044 2.051 2.442 2.301 3.144 1.999 3.057	2.232 1.531 1.874 1.989 2.492 2.141 3.102 1.981 3.072	2.127 1.488 1.963 2.055 2.435 2.269 3.147 2.041 3.083	1.307 1.499 1.799 1.726 2.392 2.075 3.025 1.911 2.894	0.029 0.729 0.331 0.239 1.478 0.493 0.058 0.860 0.771	0.014 0.114 0.060 0.040 0.211 0.053 -0.006 0.047 0.118	96 92 89 96 105 90 98 98 101	91 87 95 100 99 98 100 104 101	49 88 85 81 95 85 95 91 91	-91 -9 -23 -22 6 -34 -93 -13 -32	-96 -86 -87 -87 -93 -100 -95 -90	9.55E-7 2.47E-6 2.10E-6 3.19E-6 1.98E-6 1.73E-6 2.48E-6 2.48E-6 2.16E-6	2.24E-6 8.10E-6 6.07E-6 6.15E-6 1.15E-5 5.20E-6 3.20E-6 7.49E-6 5.48E-6	5.08E-6 3.43E-5 2.65E-5 2.71E-5 4.10E-5 1.87E-5 5.90E-6 2.81E-5 2.03E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.843 0.780 0.904 0.923 0.542 0.634 0.795	2.785 2.308 2.059 1.870 2.198 2.192 1.981	2.813 2.357 1.969 1.714 2.402 2.164 1.888	2.700 2.339 2.004 1.790 2.348 2.111 1.948	2.748 2.254 1.930 1.925 2.153 2.017 2.008	1.107 0.301 1.100 1.011 0.649 0.672 1.115	0.163 0.001 0.023 0.187 0.083 0.260 0.029	101 103 92 83 112 98 92	96 102 95 91 109 95 97	98 96 89 106 97 89 102	14 -61 17 9 6 2 27	-81 -100 -97 -80 -85 -59 -96	3.71E-6 1.97E-6 3.47E-6 3.79E-6 3.31E-6 2.81E-6 4.94E-6	1.39E-5 4.08E-6 1.41E-5 1.27E-5 1.18E-5 1.09E-5 1.65E-5	4.73E-5 8.47E-6 3.85E-5 4.63E-5 4.16E-5 7.14E-5 4.21E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.666 1.313 0.539 0.830 0.803 0.980 0.909 0.988	2.604 2.106 2.158 3.242 1.537 3.317 1.622 2.962	2.367 1.991 2.050 3.099 1.550 3.246 1.583 2.864	2.515 2.002 2.097 3.213 1.579 3.319 1.619 2.771	2.702 2.154 2.086 3.131 1.620 3.254 1.801 2.822	0.428 1.579 0.115 1.276 0.152 1.482 0.980 0.133	0.025 0.055 0.044 0.070 0.045 0.271 0.052 0.078	88 85 93 94 102 97 95 95	95 87 96 99 106 100 100 90	105 106 96 95 111 97 125 93	-36 34 -79 18 -81 21 10 -87	-96 -92 -92 -92 -94 -72 -94 -92	2.46E-6 5.93E-6 1.83E-6 3.89E-6 2.08E-6 4.20E-6 4.49E-6 1.73E-6	5.57E-6 1.82E-5 3.54E-6 1.47E-5 3.79E-6 1.69E-5 1.24E-5 3.29E-6	1.72E-5 4.42E-5 6.85E-6 4.19E-5 6.89E-6 5.78E-5 3.76E-5 6.25E-6
Prostate Cancer PC-3 DU-145	0.571 0.326	2.404 1.522	2.427 1.546	2.460 1.483	2.325 1.345	0.497 0.328	0.047 -0.011	101 102	103 97	96 85	-13	-92 -100	2.63E-6 2.59E-6	7.60E-6 1.00E-5	2.95E-5 3.17E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.400 C 0.732 1.372 1.210 0.770 0.790	2.161 1.939 2.508 2.709 1.665 1.488	1.899 1.963 2.517 2.568 1.618 1.457	1.970 2.010 2.545 2.643 1.650 1.548	1.195 1.976 2.576 2.557 1.560 1.395	0.521 1.016 2.022 1.172 0.924 0.522	0.177 0.163 1.035 0.014 0.327 0.167	85 102 101 91 95 95	89 106 103 96 98 109	45 103 106 90 88 87	7 23 57 -3 17 -34	-56 -78 -25 -99 -58 -79	7.75E-7 4.64E-6 1.22E-5 2.68E-6 3.45E-6 2.01E-6	1.29E-5 1.71E-5 5.01E-5 9.25E-6 1.70E-5 5.23E-6	8.06E-5 5.32E-5 > 1.00E-4 3.09E-5 7.93E-5 2.28E-5

		Natio	onal	Cano	er Ir	nstitu In-	ıte D ∙Vitro	evelop Testir	mer ng R	ital T esult	hera s	peutio	cs Progran	n	
NSC : D - 783	638 / 1				Exp	erimer	nt ID:1	504NS69)			Test	Гуре : 08	Units : N	lolar
Report Date :	Decemb	ber 27, 2	2015		Tes	t Date	: April	13, 2015				QNS	:	MC :	
COMI : KCN-F	PGJ-44				Sta	in Rea	gent : S	RB Dual-	Pass	Related	1	SSPL	: 0ZAS		
						Lo	og10 Cor	ncentration							
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	n Optica -6.0	l Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.574 1.047 0.333 0.964 0.812 0.493	2.151 2.962 2.405 3.110 2.991 1.678	2.074 3.041 2.375 3.126 2.854 1.659	2.021 2.920 2.175 3.194 2.857 1.520	0.922 2.605 1.216 2.801 1.660 0.975	0.594 0.882 0.300 0.753 0.747 0.426	0.452 0.625 0.167 0.756 0.785 0.369	95 104 99 101 94 98	92 98 89 104 94 87	22 81 43 86 39 41	1 -16 -22 -8 -14	-21 -40 -50 -22 -3 -25	3.97E-7 2.10E-6 6.92E-7 2.14E-6 6.28E-7 6.27E-7	1.13E-5 6.87E-6 6.44E-6 6.26E-6 6.73E-6 5.62E-6	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	Cancer 0.453 0.829 0.638 1.340 0.894 0.626 1.234 0.444 0.866	1.749 2.139 1.642 1.929 2.334 2.060 2.816 3.181 1.972	1.676 2.058 1.601 1.872 2.290 2.022 2.787 3.222 1.817	1.648 1.954 1.645 1.879 2.286 1.953 2.877 3.194 1.786	1.718 2.065 1.735 1.967 2.243 1.890 2.887 3.187 1.520	0.302 0.331 0.500 0.663 0.381 0.462 1.445 0.455 0.455	0.031 -0.011 0.048 0.034 0.552 0.126 0.067 0.154 0.141	94 96 90 97 97 98 101 86	92 86 100 92 97 93 104 100 83	98 94 109 106 94 88 104 100 59	-33 -60 -22 -51 -57 -26 13 -43	-93 -100 -93 -98 -38 -80 -95 -65 -84	2.31E-6 1.94E-6 2.84E-6 2.29E-6 1.95E-6 2.16E-6 3.96E-6 3.18E-6 1.23E-6	5.56E-6 4.08E-6 6.83E-6 4.77E-6 4.17E-6 5.89E-6 1.33E-5 1.01E-5 3.77E-6	1.89E-5 8.60E-6 2.51E-5 9.92E-6 2.77E-5 3.86E-5 5.85E-5 1.46E-5
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.359 0.425 0.319 0.264 0.380 0.437 0.686	1.466 1.461 2.718 2.002 1.912 2.452 3.195	1.464 1.570 2.705 1.907 1.935 2.465 3.158	1.421 1.546 2.455 1.763 1.974 2.477 3.175	1.173 1.578 0.632 1.281 1.215 2.141 3.092	0.197 0.037 0.117 0.165 0.196 0.103 0.657	0.095 0.032 0.012 0.008 0.062 0.052 0.238	100 110 99 95 102 101 99	96 108 89 86 104 101 99	73 111 13 58 55 85 96	-45 -91 -63 -38 -48 -77 -4	-74 -93 -96 -97 -84 -88 -65	1.58E-6 2.01E-6 3.26E-7 1.23E-6 1.11E-6 1.64E-6 2.87E-6	4.16E-6 3.54E-6 1.48E-6 4.07E-6 3.39E-6 3.35E-6 9.06E-6	1.47E-5 6.25E-6 6.67E-6 1.62E-5 1.11E-5 6.84E-6 5.61E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.763 0.867 1.112 0.565 0.683 0.592	2.400 2.779 2.887 2.168 1.634 2.159	2.375 2.722 2.861 2.090 1.535 2.084	2.424 2.676 2.792 2.082 1.460 2.038	2.340 2.730 2.891 1.919 1.509 1.598	0.699 0.476 0.889 0.479 0.449 0.136	0.052 0.042 0.111 0.147 0.035 0.027	98 97 99 95 90 95	101 95 95 82 92	96 97 100 84 87 64	-8 -45 -20 -15 -34 -77	-93 -95 -90 -74 -95 -96	2.77E-6 2.15E-6 2.61E-6 2.22E-6 2.02E-6 1.26E-6	8.30E-6 4.83E-6 6.81E-6 7.04E-6 5.21E-6 2.85E-6	3.09E-5 1.25E-5 2.68E-5 3.90E-5 1.82E-5 6.43E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.331 0.800 0.432 0.305 1.421 0.745 0.820 0.990 1.140	2.425 1.555 1.991 2.040 2.450 2.312 3.196 1.846 3.058	2.312 1.541 1.905 2.003 2.505 2.315 3.163 1.782 2.981	2.065 1.506 1.753 1.878 2.539 2.257 3.105 1.780 2.925	0.997 1.444 1.611 0.817 2.359 2.290 3.039 1.773 2.800	0.034 0.681 0.309 0.187 0.849 0.594 0.025 0.627 1.001	0.010 0.135 0.065 0.014 0.136 0.110 -0.006 0.096 0.213	95 98 94 105 100 99 93 96	83 94 85 91 109 96 92 93	32 85 76 30 91 99 93 92 87	-90 -15 -29 -39 -40 -20 -97 -37 -12	-97 -83 -96 -90 -85 -100 -90 -81	4.39E-7 2.25E-6 1.76E-6 4.62E-7 2.06E-6 2.56E-6 1.69E-6 2.11E-6 2.34E-6	1.82E-6 7.10E-6 5.32E-6 2.70E-6 4.94E-6 6.75E-6 3.09E-6 5.18E-6 7.52E-6	4.70E-6 3.27E-5 2.39E-5 1.57E-5 1.56E-5 2.86E-5 5.66E-6 1.77E-5 3.52E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.843 0.780 0.904 0.923 0.542 0.634 0.795	2.806 2.340 2.181 1.934 2.026 2.340 1.959	2.884 2.417 2.202 1.930 2.071 2.392 1.942	2.908 2.446 2.072 1.917 2.033 2.311 1.882	2.793 1.935 2.013 2.146 0.955 1.369 2.016	0.825 0.223 1.199 0.964 0.492 0.673 0.691	0.198 -0.020 0.076 0.238 0.106 0.373 -0.002	104 105 102 100 103 103 98	105 107 91 98 100 98 93	99 74 87 121 28 43 105	-2 -71 23 4 -9 2 -13	-77 -100 -92 -74 -80 -41 -100	3.06E-6 1.46E-6 3.78E-6 4.05E-6 4.95E-7 7.48E-7 2.92E-6	9.53E-6 3.23E-6 1.59E-5 1.13E-5 5.63E-6 1.13E-5 7.75E-6	4.40E-5 7.13E-6 4.34E-5 4.90E-5 3.74E-5 > 1.00E-4 2.66E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.666 1.313 0.539 0.830 0.803 0.980 0.909 0.988	2.461 2.144 2.178 3.360 1.541 3.246 1.632 2.951	2.411 2.070 2.223 3.308 1.550 3.188 1.572 2.889	2.474 2.000 2.166 3.214 1.549 3.225 1.754 2.849	2.566 2.061 1.538 3.181 1.473 3.282 1.802 2.659	0.125 0.167 0.076 1.391 0.042 1.207 0.461 0.066	0.017 0.036 0.058 0.111 0.032 0.182 -0.003 0.068	97 91 103 98 101 97 92 97	101 83 99 94 101 99 117 95	106 90 61 93 91 102 124 85	-81 -87 -86 22 -95 10 -49 -93	-97 -89 -87 -96 -81 -100 -93	1.99E-6 1.68E-6 1.19E-6 4.04E-6 3.66E-6 3.66E-6 2.66E-6 1.57E-6	3.68E-6 3.22E-6 2.60E-6 1.60E-5 3.08E-6 1.29E-5 5.19E-6 3.00E-6	6.80E-6 6.16E-6 5.69E-6 4.60E-5 5.73E-6 4.53E-5 1.03E-5 5.72E-6
Prostate Cancer PC-3 DU-145	0.571 0.326	2.395 1.480	2.306 1.514	2.313 1.507	2.026 1.192	0.353 0.201	0.046 -0.014	95 103	95 102	80 75	-38 -38	-92 -100	1.79E-6 1.66E-6	4.74E-6 4.58E-6	1.65E-5 1.54E-5
Breast Cancer MCF7 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.400 C 0.732 1.372 1.210 0.770 0.790	2.151 1.834 2.580 2.764 1.621 1.515	2.007 1.820 2.527 2.712 1.587 1.496	1.648 1.747 2.541 2.597 1.416 1.498	0.836 1.772 2.627 2.634 1.372 1.395	0.258 1.013 1.668 1.090 0.676 0.291	0.125 0.200 1.262 0.026 0.237 0.227	92 99 96 97 96 97	71 92 97 89 76 98	25 94 104 92 71 83	-36 25 25 -10 -12 -63	-69 -73 -8 -98 -69 -71	2.87E-7 4.41E-6 4.78E-6 2.57E-6 1.78E-6 1.69E-6	2.58E-6 1.82E-5 5.67E-5 7.99E-6 7.11E-6 3.71E-6	2.71E-5 5.87E-5 > 1.00E-4 2.86E-5 4.60E-5 8.12E-6

		Natio	onal	Cano	er Ir	nstitu In-	ite De Vitro	evelop Testir	omer ng R	ital T esult	hera s	peutic	s Progran	n	
NSC : D - 782	138 / 1				Exp	erimer	nt ID:1	410NS77	,			Test T	ype : 08	Units : N	Iolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Octob	er 27, 20	14			QNS :		MC :	
COMI : KCN-F	PGJ-14				Sta	in Rea	gent : S	RB Dual	Pass	Related		SSPL	: 0ZAS		
	Log10 Concentration														
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	o Optica -6.0	l Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.340 0.973 0.334 0.644 0.758 0.284	1.576 3.268 2.828 2.417 2.735 1.723	1.540 3.234 2.814 2.424 2.675 1.661	1.502 3.207 2.799 2.428 2.671 1.574	1.245 3.125 2.569 2.232 2.442 1.448	0.393 0.978 0.597 0.679 0.789 0.312	0.256 0.544 0.379 0.481 0.628 0.265	97 99 99 100 97 96	94 97 99 101 97 90	73 94 90 90 85 81	4 11 2 2 2	-25 -44 2 -25 -17 -7	2.17E-6 2.93E-6 3.17E-6 2.83E-6 2.63E-6 2.46E-6	1.40E-5 1.01E-5 > 1.00E-4 1.18E-5 1.21E-5 1.67E-5	> 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H220 NCI-H460 NCI-H522	Cancer 0.444 0.724 0.644 1.250 1.157 0.578 1.071 0.190 1.254	1.938 1.912 1.873 1.730 2.560 1.998 2.482 2.451 2.717	1.831 1.847 1.829 1.634 2.463 1.943 2.373 2.505 2.626	1.869 1.779 1.781 1.636 2.561 1.934 2.485 2.500 2.651	1.891 1.857 1.896 1.734 2.665 1.884 2.503 2.566 2.480	1.355 1.616 0.546 1.451 0.781 0.911 1.691 0.433 0.487	0.355 0.146 0.144 0.091 1.153 0.132 0.094 0.201 0.070	93 95 96 80 93 96 92 102 94	95 89 93 80 100 95 100 102 96	97 95 102 101 107 92 102 105 84	61 75 -15 42 -32 23 44 11 -61	-20 -80 -78 -93 -77 -91 -94	1.36E-5 1.45E-5 2.77E-6 7.26E-6 2.57E-6 4.09E-6 7.84E-6 3.84E-6 1.71E-6	5.66E-5 3.05E-5 7.40E-6 2.04E-5 5.86E-6 1.71E-5 2.11E-5 > 1.00E-4 3.78E-6	> 1.00E-4 6.42E-5 3.60E-5 4.81E-5 > 1.00E-4 5.37E-5 4.95E-5 > 1.00E-4 8.37E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.558 0.701 0.520 0.225 0.422 0.465 0.239	2.063 2.827 3.253 1.721 2.282 3.101 2.484	2.103 2.651 3.280 1.612 2.221 3.027 2.341	2.096 2.915 3.172 1.583 2.458 3.127 2.436	2.281 3.032 3.187 1.541 2.479 2.927 2.512	0.600 0.253 0.251 0.491 0.528 0.574 0.740	0.171 0.062 0.040 0.057 0.036 0.168 0.230	103 92 101 93 97 97 94	102 104 97 91 109 101 98	114 110 98 88 111 93 101	3 -64 -52 18 6 4 22	-69 -91 -92 -75 -91 -64 -4	3.78E-6 2.21E-6 3.47E-6 3.78E-6 3.78E-6 3.06E-6 4.46E-6	1.09E-5 4.28E-6 4.50E-6 1.56E-5 1.14E-5 1.15E-5 7.06E-5	5.39E-5 8.31E-6 9.74E-6 5.41E-5 3.74E-5 6.25E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.518 0.944 1.012 0.799 0.973 0.760	1.831 2.981 2.958 2.552 1.883 2.487	1.789 2.835 2.872 2.406 1.707 2.391	1.837 2.831 2.872 2.443 1.593 2.402	1.671 3.066 2.966 2.454 1.652 2.475	0.978 1.834 1.290 1.628 1.446 0.926	0.358 0.177 0.362 0.198 0.372 0.002	97 93 96 92 81 94	100 93 96 94 68 95	88 104 100 94 75 99	35 44 14 47 52 10	-31 -81 -64 -75 -62 -100	5.20E-6 7.86E-6 3.85E-6 8.75E-6 1.04E-5 3.54E-6	3.40E-5 2.24E-5 1.52E-5 2.43E-5 2.86E-5 1.22E-5	> 1.00E-4 5.62E-5 6.59E-5 6.22E-5 7.88E-5 3.51E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.293 0.805 0.473 0.492 1.312 0.623 1.114 1.117 0.587	2.138 1.784 2.006 2.651 2.384 1.869 3.046 2.221 2.593	2.114 1.713 1.973 2.610 2.386 1.876 2.926 2.100 2.330	2.123 1.717 1.828 2.482 2.355 1.816 3.018 2.106 2.286	1.878 1.706 1.799 2.482 2.300 1.952 3.022 2.101 2.056	0.106 0.943 0.556 0.627 1.435 0.742 0.798 1.508 0.542	0.028 0.332 0.171 0.130 0.213 0.199 0.036 0.119 0.244	99 93 98 98 100 101 94 89 87	99 93 88 92 97 96 99 90 85	86 92 87 92 92 107 99 89 73	-64 14 5 11 10 -28 35 -8	-91 -59 -64 -74 -84 -68 -97 -89 -59	1.74E-6 3.46E-6 2.82E-6 3.10E-6 3.83E-6 3.83E-6 2.42E-6 5.35E-6 1.94E-6	3.74E-6 1.56E-5 1.20E-5 1.32E-5 1.32E-5 5.98E-6 1.92E-5 8.02E-6	8.07E-6 7.58E-5 6.29E-5 5.06E-5 4.42E-5 5.85E-5 2.07E-5 4.84E-5 6.80E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.881 0.472 0.677 0.725 0.604 0.586 0.850	2.571 1.938 1.718 2.203 2.341 2.045 1.670	2.554 1.978 1.754 2.169 2.292 2.075 1.673	2.634 1.952 1.603 2.131 2.283 2.104 1.660	2.650 1.809 1.533 2.348 2.349 2.050 1.855	1.539 0.625 0.990 1.318 0.759 0.613 1.509	0.393 0.052 0.207 0.407 0.281 0.630 0.271	99 103 103 98 97 102 100	104 101 89 95 97 104 99	105 91 82 110 100 123	39 10 30 40 9 2 80	-55 -89 -69 -44 -54 3 -68	6.78E-6 3.23E-6 4.15E-6 7.22E-6 3.56E-6 3.56E-6 3.24E-6 1.60E-5	2.59E-5 1.27E-5 2.00E-5 3.00E-5 1.39E-5 > 1.00E-4 3.47E-5	8.77E-5 4.05E-5 6.38E-5 > 1.00E-4 8.77E-5 > 1.00E-4 7.54E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.788 1.169 0.537 0.594 1.270 0.664 0.886 0.987	2.793 2.108 2.319 2.781 1.957 2.611 2.018 2.664	2.772 2.087 2.362 2.644 1.858 2.509 1.949 2.426	2.714 2.121 2.275 2.539 1.884 2.486 1.987 2.553	2.847 2.234 2.338 2.767 1.954 2.480 2.096 2.556	0.540 1.972 1.009 1.446 1.190 0.965 1.386 1.617	0.134 0.142 0.145 0.127 0.066 0.605 0.074 0.149	99 98 102 94 85 95 94 86	96 101 98 89 89 94 97 93	103 113 101 99 100 93 107 94	-31 85 26 39 -6 15 44 38	-83 -73 -79 -95 -9 -92 -85	2.47E-6 1.60E-5 4.84E-6 6.56E-6 2.94E-6 3.60E-6 8.06E-6 5.99E-6	5.83E-6 3.11E-5 1.85E-5 2.14E-5 8.71E-6 4.31E-5 2.11E-5 2.03E-5	2.29E-5 6.05E-5 5.86E-5 5.70E-5 3.11E-5 > 1.00E-4 4.93E-5 5.19E-5
Prostate Cancer PC-3 DU-145	0.736 0.413	1.740 1.764	1.653 1.783	1.715 1.757	1.853 1.690	1.065 0.847	0.253 0.070	91 101	98 100	111 95	33 32	-66 -83	6.03E-6 5.17E-6	2.15E-5 1.90E-5	6.94E-5 5.16E-5
Breast Cancer MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.396 C 0.568 0.973 1.343 0.680 0.703	2.207 1.433 1.940 2.748 1.432 1.346	2.011 1.409 1.876 2.775 1.387 1.282	1.944 1.488 1.874 2.652 1.341 1.318	1.730 1.531 1.972 2.724 1.360 1.280	0.822 0.941 1.604 1.287 0.844 0.571	0.140 0.435 1.278 0.228 0.339 0.172	89 97 93 102 94 90	86 106 93 93 88 96	74 111 103 98 90 90	24 43 65 -4 22 -19	-65 -24 32 -83 -50 -76	2.96E-6 7.94E-6 2.84E-5 2.96E-6 3.88E-6 2.32E-6	1.85E-5 4.44E-5 > 1.00E-4 9.10E-6 2.01E-5 6.71E-6	6.82E-5 > 1.00E-4 > 1.00E-4 3.81E-5 9.93E-5 3.54E-5

		Natio	onal	Cano	er Ir	nstitu In-	ite Do Vitro	evelop Testir	men ng R	ital T esult	hera s	peuti	cs Program	1	
NSC : D - 782	139 / 1				Exp	erimer	nt ID : 1	410NS77	,			Test	Туре : 08	Units : N	Iolar
Report Date :	Decemb	ber 27, 2	2015		Tes	t Date	: Octob	oer 27, 20	14			QNS	:	MC :	
COMI : KCN-F	PGJ-15				Sta	in Rea	gent : S	RB Dual-	Pass I	Related	I	SSPL	: 0ZAS		
						L	og10 Cor	ncentration				•		•	
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.0	Mear -7.0	n Optica -6.0	I Densiti -5.0	es -4.0	-8.0	P -7.0	ercent G -6.0	Frowth -5.0	-4.0	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.340 0.973 0.334 0.644 0.758 0.284	1.563 3.163 2.666 2.404 2.681 1.667	1.507 3.101 2.697 2.442 2.687 1.550	1.479 3.072 2.607 2.371 2.678 1.456	0.422 2.534 1.106 1.648 1.413 0.384	0.272 0.781 0.404 0.442 0.718 0.230	0.200 0.477 0.240 0.420 0.502 0.183	95 97 101 102 100 92	93 96 97 98 100 85	7 71 33 57 34 7	-20 -20 -31 -5 -19	-41 -51 -28 -35 -34 -36	3.15E-7 1.71E-6 5.46E-7 1.20E-6 5.72E-7 2.81E-7	1.77E-6 6.06E-6 1.25E-5 4.41E-6 7.32E-6 1.87E-6	 > 1.00E-4 9.27E-5 > 1.00E-4 > 1.00E-4 > 1.00E-4 > 1.00E-4
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H460 NCI-H522	Cancer 0.444 0.724 0.644 1.250 1.157 0.578 1.071 0.190 1.254	1.945 1.895 1.740 1.724 2.283 1.803 2.423 2.405 2.740	1.923 1.786 1.671 1.641 2.168 1.791 2.412 2.406 2.614	1.946 1.730 1.662 1.665 2.383 1.866 2.405 2.474 2.594	1.964 1.844 1.495 1.763 2.263 1.732 2.383 2.400 2.021	0.294 0.771 0.329 0.867 0.329 0.370 1.096 0.217 0.169	0.056 -0.008 0.080 0.100 0.566 0.125 0.033 0.114 0.100	99 91 94 82 90 99 99 100 92	100 86 93 88 109 105 99 103 90	101 96 78 108 98 94 97 100 52	-34 49 -31 -72 -36 2 1 -87	-87 -100 -88 -92 -51 -78 -97 -40 -92	2.40E-6 3.15E-6 1.65E-6 2.62E-6 1.92E-6 3.12E-6 3.20E-6 1.03E-6	5.62E-6 1.09E-5 4.10E-6 6.02E-6 3.79E-6 5.29E-6 1.04E-5 1.07E-5 2.36E-6	2.01E-5 3.30E-5 1.06E-5 2.07E-5 7.46E-6 2.13E-5 3.35E-5 > 1.00E-4 5.44E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.558 0.701 0.520 0.225 0.422 0.465 0.239	2.025 2.549 3.144 1.612 2.185 3.126 2.442	2.059 2.414 3.173 1.560 2.207 3.145 2.357	2.016 2.624 3.030 1.433 2.423 3.171 2.427	1.843 2.846 1.735 0.691 1.754 2.557 1.248	0.201 0.013 0.090 0.100 0.112 0.309 0.248	0.137 0.026 0.015 0.031 0.112 0.118 0.164	102 93 101 96 101 101 96	99 104 96 87 114 102 99	88 116 46 34 76 79 46	-64 -98 -83 -56 -74 -34	-76 -96 -97 -86 -73 -75 -32	1.77E-6 2.03E-6 8.41E-7 4.94E-7 1.48E-6 1.80E-6 8.34E-7	3.78E-6 3.48E-6 2.28E-6 2.38E-6 3.21E-6 5.02E-6 1.03E-5	8.08E-6 5.96E-6 8.62E-6 6.95E-6 2.51E-5 > 1.00E-4
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.518 0.944 1.012 0.799 0.973 0.760	1.852 2.993 2.809 2.540 1.952 2.518	1.821 2.918 2.795 2.382 1.782 2.404	1.797 2.875 2.769 2.452 1.694 2.438	1.618 2.931 2.857 2.278 1.702 2.120	0.565 0.631 0.727 1.021 1.539 0.049	0.080 0.022 0.080 0.150 0.098 0.001	98 96 99 91 83 94	96 94 98 95 74 95	82 97 103 85 74 77	3 -33 -28 13 58 -94	-85 -98 -92 -81 -90 -100	2.57E-6 2.30E-6 2.53E-6 3.05E-6 1.13E-5 1.45E-6	1.10E-5 5.56E-6 6.09E-6 1.37E-5 2.46E-5 2.83E-6	4.05E-5 1.82E-5 2.19E-5 4.65E-5 5.37E-5 5.56E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.293 0.805 0.473 0.492 1.312 0.623 1.114 1.117 0.587	1.970 1.742 1.859 2.637 2.331 1.861 2.775 2.228 2.542	1.949 1.660 1.778 2.549 2.275 1.820 2.673 2.084 2.222	1.856 1.681 1.687 2.494 2.313 1.797 2.794 2.017 2.227	0.172 1.599 1.439 1.688 2.170 1.686 2.499 2.065 1.452	0.014 0.497 0.201 0.422 0.509 0.269 0.053 0.570 0.276	0.037 0.216 0.045 0.110 0.087 0.100 0.072 0.018 0.163	99 91 94 96 94 97 94 87 84	93 93 93 93 98 95 101 81 84	-41 85 70 56 84 86 83 85 44	-95 -38 -58 -14 -61 -57 -95 -49 -53	-87 -73 -90 -78 -93 -84 -94 -98 -72	2.10E-7 1.92E-6 1.43E-6 1.21E-6 1.72E-6 1.78E-6 1.54E-6 1.83E-6 7.15E-7	4.93E-7 4.88E-6 3.53E-6 6.26E-6 3.79E-6 4.00E-6 2.93E-6 4.32E-6 2.85E-6	1.45E-6 2.16E-5 8.73E-6 3.67E-5 8.37E-6 8.96E-6 5.58E-6 1.05E-5 9.32E-6
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.881 0.472 0.677 0.725 0.604 0.586 0.850	2.533 1.943 1.735 2.147 2.459 1.907 1.585	2.569 1.961 1.718 2.127 2.402 1.925 1.574	2.594 2.033 1.687 2.090 2.366 1.953 1.538	2.565 1.118 1.545 2.215 1.427 1.514 1.765	0.776 0.074 0.988 0.582 0.810 0.525 1.007	0.178 0.226 0.146 0.083 0.392 0.003	102 101 98 99 97 101 98	104 106 95 96 95 103 94	102 44 82 105 44 70 124	-12 -84 29 -20 11 -10 21	-80 -100 -67 -80 -86 -33 -100	2.86E-6 7.99E-7 4.06E-6 2.75E-6 7.74E-7 1.78E-6 5.27E-6	7.86E-6 2.20E-6 2.02E-5 6.94E-6 1.30E-5 7.41E-6 1.50E-5	3.64E-5 5.39E-6 6.71E-5 3.18E-5 4.24E-5 > 1.00E-4 3.88E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.788 1.169 0.537 0.594 1.270 0.664 0.886 0.987	2.735 2.057 2.298 2.835 1.846 2.577 2.034 2.622	2.720 2.042 2.312 2.563 1.785 2.448 2.010 2.370	2.623 2.061 2.178 2.543 1.860 2.534 1.999 2.448	2.654 2.250 2.121 2.542 1.883 2.252 2.110 2.341	0.161 0.465 0.112 0.990 0.199 0.428 0.764 0.106	0.005 0.041 0.056 0.047 0.107 0.311 0.011 0.035	99 98 101 88 89 93 98 85	94 100 93 87 102 98 97 89	96 122 90 87 106 83 107 83	-80 -60 -79 18 -84 -36 -14 -89	-99 -97 -90 -92 -53 -99 -97	1.82E-6 2.48E-6 1.72E-6 3.41E-6 1.97E-6 1.90E-6 2.95E-6 1.55E-6	3.52E-6 4.67E-6 3.40E-6 1.45E-5 3.61E-6 5.01E-6 7.68E-6 3.03E-6	6.78E-6 8.79E-6 6.72E-6 4.13E-5 6.60E-6 6.55E-5 2.66E-5 5.91E-6
Prostate Cancer PC-3 DU-145	0.736 0.413	1.725 1.765	1.656 1.757	1.718 1.751	1.705 1.601	0.583 0.680	0.090 -0.005	93 99	99 99	98 88	-21 20	-88 -100	2.53E-6 3.60E-6	6.68E-6 1.46E-5	2.73E-5 3.82E-5
Breast Cancer MCF7 HS -MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.396 C 0.568 0.973 1.343 0.680 0.703	2.240 1.443 1.940 2.605 1.381 1.258	2.120 1.493 1.852 2.632 1.374 1.212	1.928 1.471 1.879 2.521 1.280 1.303	0.748 1.399 1.977 2.464 1.204 1.119	0.366 0.576 1.341 0.558 0.666 0.175	0.179 0.236 0.790 -0.004 0.387 0.135	93 106 91 102 99 92	83 103 94 93 86 108	19 95 104 89 75 75	-8 1 38 -58 -2 -75	-55 -59 -19 -100 -43 -81	3.29E-7 3.00E-6 6.59E-6 1.83E-6 2.10E-6 1.47E-6	5.20E-6 1.03E-5 4.67E-5 4.01E-6 9.38E-6 3.16E-6	7.91E-5 7.18E-5 > 1.00E-4 8.76E-6 > 1.00E-4 6.80E-6

		Natio	onal	Cano	er Ir	nstitu In-	ite D -Vitro	evelop Testii	omer ng R	ntal T esult	hera s	peuti	cs Program	l	
NSC : D - 788	3106 / 1				Exp	erimer	nt ID : 1	512NS26	3			Test	Туре : 08	Units : N	Iolar
Report Date :	Februar	ry 08, 20)16		Tes	t Date	: Dece	mber 20,	2015			QNS	:	MC :	
COMI : KCN-	PGJ-58				Sta	in Rea	gent : S	SRB Dual	-Pass I	Related	1	SSP	L:0ZAS		
	Log10 Concentration													·	
Panel/Cell Line	Time Zero	Ctrl	-8.5	Mear -7.5	o Optica -6.5	I Densiti -5.5	ies -4.5	-8.5	P -7.5	ercent G -6.5	Fowth -5.5	-4.5	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.564 1.034 0.258 0.567 0.864 0.327	2.243 2.441 1.758 2.110 2.341 1.538	2.179 2.635 1.751 2.033 2.327 1.500	2.375 2.575 1.757 2.057 2.443 1.543	2.250 2.701 1.767 1.981 2.260 1.368	0.660 1.004 0.378 0.610 0.736 0.388	0.498 0.946 0.232 0.452 0.584 0.386	96 114 100 95 99 97	108 110 100 97 107 100	100 118 101 92 95 86	6 -3 8 3 -15 5	-12 -9 -10 -20 -32 5	1.13E-6 1.22E-6 1.17E-6 9.76E-7 8.47E-7 9.24E-7	7.05E-6 3.14E-6 9.10E-6 4.37E-6 2.43E-6 > 3.32E-5	 > 3.32E-5
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.329 0.709 0.869 1.598 1.106 0.631 0.715 0.243 1.165	1.265 2.058 1.909 1.986 2.717 1.946 2.155 2.538 2.010	1.223 1.927 1.811 1.949 2.646 1.851 2.044 2.580 1.950	1.290 1.951 1.928 1.979 2.678 1.808 2.127 2.712 1.871	1.260 1.979 1.936 2.021 2.707 1.744 2.183 2.545 1.781	0.441 1.076 0.943 1.826 0.958 0.588 1.644 0.750 0.671	0.292 0.418 0.511 0.647 1.189 0.226 0.017 0.219 0.110	95 90 91 90 96 93 92 102 93	103 92 102 98 90 98 108 84	99 94 103 109 99 85 102 100 73	12 27 7 59 -13 -7 64 22 -42	-11 -41 -60 5 -64 -98 -10 -91	1.22E-6 1.51E-6 1.18E-6 9.10E-7 7.93E-7 4.08E-6 1.46E-6 5.24E-7	1.09E-5 8.30E-6 4.65E-6 1.04E-5 2.79E-6 8.30E-6 1.63E-5 1.42E-6	> 3.32E-5 > 3.32E-5 > 3.32E-5 2.76E-5 > 3.32E-5 1.88E-5 1.69E-5 > 3.32E-5 4.77E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 SW-620	0.450 0.764 0.315 0.356 0.281 0.245	1.394 2.482 2.154 2.147 1.285 1.668	1.424 2.413 2.088 1.944 1.242 1.782	1.429 2.396 2.102 2.045 1.222 1.889	1.459 2.470 1.944 1.913 1.291 1.923	0.413 0.624 0.162 0.285 0.206 0.537	0.129 0.075 0.027 0.095 0.032 0.102	103 96 99 96 108	104 95 97 94 94 115	107 99 89 87 101 118	-8 -18 -49 -20 -27 21	-71 -90 -91 -73 -89 -58	1.04E-6 8.71E-7 6.34E-7 7.35E-7 8.28E-7 1.65E-6	2.82E-6 2.32E-6 1.47E-6 2.15E-6 2.04E-6 6.04E-6	1.52E-5 9.14E-6 3.56E-6 1.21E-5 7.87E-6 2.60E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.589 0.799 1.079 0.772 0.954 0.346	2.084 2.737 2.855 2.508 1.668 1.252	2.003 2.466 2.763 2.301 1.378 1.225	2.015 2.540 2.765 2.306 1.395 1.271	2.030 2.648 2.749 2.273 1.393 1.293	0.992 1.462 1.109 1.625 1.262 0.386	0.386 0.205 0.078 0.217 0.075 0.030	95 86 95 88 59 97	95 90 95 88 62 102	96 95 94 86 61 104	27 34 2 49 43 4	-35 -74 -93 -72 -92 -91	1.54E-6 1.83E-6 9.95E-7 3.15E-6 1.40E-6 1.16E-6	9.10E-6 6.86E-6 3.46E-6 8.45E-6 6.92E-6 3.69E-6	> 3.32E-5 1.98E-5 1.17E-5 2.19E-5 1.62E-5 1.62E-5 1.23E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.493 0.845 0.628 0.598 0.820 0.705 0.812 0.963 0.761	2.953 1.831 2.111 2.835 1.247 1.863 2.997 1.740 2.658	2.811 1.803 2.027 2.704 1.287 1.860 2.924 1.731 2.509	2.785 1.832 2.014 2.842 1.269 1.845 2.951 1.738 2.577	2.676 1.807 1.931 2.742 1.234 1.865 2.834 1.724 2.406	0.097 1.199 0.778 0.547 0.694 0.688 0.627 1.225 0.653	0.038 0.358 0.246 0.199 0.167 0.149 0.038 0.415 0.135	94 97 94 109 100 97 99 92	93 100 93 100 105 98 98 100 96	89 98 88 96 97 100 93 98 87	-80 36 10 -9 -15 -2 -23 34 -14	-92 -58 -61 -67 -80 -79 -95 -57 -82	5.63E-7 1.96E-6 9.12E-7 8.71E-7 1.02E-6 7.76E-7 1.85E-6 7.67E-7	1.11E-6 8.04E-6 4.61E-6 2.75E-6 3.15E-6 2.10E-6 7.82E-6 2.40E-6	2.20E-6 2.75E-5 2.33E-5 1.71E-5 1.15E-5 1.39E-5 7.86E-6 2.78E-5 1.11E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.722 0.409 0.700 0.583 0.540 0.584 0.677	2.446 1.393 1.699 1.510 1.726 2.047 1.256	2.538 1.436 1.593 1.470 1.739 2.038 1.227	2.537 1.403 1.602 1.475 1.777 2.001 1.261	2.545 1.396 1.578 1.580 1.783 1.948 1.312	1.124 0.431 0.947 0.705 0.567 0.411 1.184	0.217 0.063 0.128 0.219 0.430 0.541 0.513	105 104 89 96 101 99 95	105 101 90 96 104 97 101	106 100 88 108 105 93 110	23 2 25 13 2 -30 87	-70 -85 -82 -63 -20 -7 -24	1.57E-6 1.08E-6 1.32E-6 1.35E-6 1.14E-6 7.47E-7 7.19E-6	5.90E-6 3.52E-6 5.66E-6 4.95E-6 4.18E-6 1.91E-6 2.01E-5	2.03E-5 1.32E-5 1.67E-5 2.27E-5 > 3.32E-5 > 3.32E-5 > 3.32E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.761 1.358 0.480 0.655 0.996 0.940 0.937 0.913	2.228 2.487 1.721 3.042 1.854 3.089 1.527 2.415	2.109 2.432 1.741 2.974 1.834 2.969 1.468 2.263	2.174 2.582 1.671 3.097 1.829 2.971 1.480 2.392	2.290 2.542 1.778 3.088 1.804 2.945 1.627 2.363	1.018 2.351 0.213 0.987 0.538 1.186 0.945 1.222	0.136 0.097 0.172 0.423 0.058 0.817 0.099 0.015	92 95 102 97 98 94 90 90	96 108 96 102 97 95 92 98	104 105 105 102 94 93 117 97	17 88 -56 14 -46 11 1 21	-82 -93 -64 -35 -94 -13 -89 -98	1.40E-6 5.38E-6 7.27E-7 1.29E-6 6.86E-7 1.12E-6 1.26E-6 1.36E-6	4.97E-6 1.02E-5 1.49E-6 6.35E-6 1.56E-6 9.69E-6 3.43E-6 4.94E-6	1.58E-5 1.92E-5 3.06E-6 > 3.32E-5 4.01E-6 > 3.32E-5 1.22E-5 1.30E-5
Prostate Cancer PC-3 DU-145	0.785 0.321	1.832 1.626	1.810 1.606	1.872 1.550	1.842 1.532	0.872 0.524	0.300 0.097	98 98	104 94	101 93	8 16	-62 -70	1.18E-6 1.19E-6	4.36E-6 5.04E-6	2.25E-5 1.94E-5
Breast Cancer MCF7 MDA-MB-231/ATC HS 578T BT-549 MDA-MB-468	0.510 C 0.664 1.143 1.144 1.213	2.691 1.888 2.376 2.239 2.383	2.400 1.773 2.468 2.133 2.345	2.441 1.821 2.513 2.217 2.402	2.155 1.799 2.433 2.247 2.287	0.923 0.773 1.901 1.176 1.065	0.335 0.496 1.364 0.274 0.497	87 91 107 90 97	89 95 111 98 102	75 93 105 101 92	19 9 61 3 -12	-34 -25 18 -76 -59	9.36E-7 1.07E-6 6.08E-6 1.10E-6 8.37E-7	7.51E-6 6.03E-6 > 3.32E-5 3.61E-6 2.53E-6	 > 3.32E-5 > 3.32E-5 > 3.32E-5 1.55E-5 2.13E-5

Developmental Ther	apeutics Program	NSC: D-786059 / 1	Conc: 1.00E-5 Molar	Test Date: Aug 10, 2015
One Dose Me	an Graph	Experiment ID: 1508	OS37	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Perc	cent
Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H23 NCI-H322M NCI-H322M NCI-H322M NCI-H322Z Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251 Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-28 SK	2.58 19.38 3.74 40.52 14.68 10.92 100.07 63.93 96.75 98.31 89.65 70.24 94.51 97.75 -68.10 47.63 76.44 -88.56 16.16 18.67 46.40 2.12 55.95 89.18 65.96 74.74 71.74 71.74 71.752 4.09 21.69 35.69 19.34 53.95 43.69 69.14 1.46 82.70 28.94 63.24 97.12 10.94 57.10 19.34 53.95 43.69 69.14 1.46 82.70 28.94 63.24 97.12 10.94 57.10 19.34 53.95 43.69 69.14 1.46 82.70 28.94 63.24 97.12 10.94 57.10 19.34 53.95 43.69 69.14 1.46 82.70 28.94 63.24 97.12 10.94 57.10 19.08 64.15 22.78 78.90 64.23 43.72 75.85 26.30 43.46 75.90 58.52 56.90 41.05 1.05			
Deita Range	222.59			
	150	100 50	0 -50	-100 -150

		Nati	onal	Cano	cer Ir	nstitu In-	ite D -Vitro	evelop Testii	omer ng R	ital T esult	hera s	peutio	cs Program	ו	
NSC : D - 786	054 / 1				Exp	erimer	nt ID : 1	509NS56	6			Test	Гуре : 08	Units : N	/lolar
Report Date :	Decemt	ber 27, 2	2015		Tes	t Date	: Septe	ember 08,	2015			QNS	:	MC :	
COMI : KCN-F	PGJ-46				Sta	in Rea	gent : S	SRB Dual	-Pass I	Related	ł	SSPL	: 0ZAS		
	T :				0	Lo	og10 Co	ncentration							
Panel/Cell Line	Zero	Ctrl	-8.8	Mear -7.8	-6.8	-5.8	-4.8	-8.8	-7.8	ercent G -6.8	-5.8	-4.8	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.854 0.734 0.259 0.951 0.482 0.285	3.339 3.171 2.584 3.315 1.727 0.873	3.316 3.130 2.548 3.277 1.759 0.870	3.346 3.115 2.497 3.287 1.687 0.806	2.890 2.860 1.694 3.064 1.203 0.495	0.867 0.766 0.379 0.999 0.375 0.290	0.570 0.580 0.291 0.686 0.312 0.223	99 98 98 98 103 99	100 98 96 99 97 88	82 87 62 89 58 36	1 5 2 -22 1	-33 -21 -28 -35 -22	4.12E-7 4.53E-7 2.69E-7 4.72E-7 2.10E-7 8.93E-8	1.73E-6 1.91E-6 > 1.67E-5 1.95E-6 8.80E-7 1.81E-6	> 1.67E-5 > 1.67E-5 > 1.67E-5 > 1.67E-5 > 1.67E-5 > 1.67E-5 > 1.67E-5
Non-Small Cell Lung A549/ATCC EKVX HOP-82 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.397 0.829 0.551 1.496 0.568 0.617 0.662 0.217 0.922	2.097 2.115 1.674 1.999 1.530 1.773 1.870 2.547 2.553	2.033 2.097 1.689 1.934 1.510 1.720 1.837 2.665 2.443	2.044 2.090 1.661 1.915 1.456 1.731 1.820 2.616 2.453	2.044 2.067 1.558 1.931 1.432 1.698 1.793 2.425 2.245	1.620 1.316 0.669 1.891 0.677 0.684 1.414 0.436 0.310	0.246 0.170 0.159 0.387 0.141 0.152 0.088 0.072 0.290	96 99 101 87 98 95 97 105 93	97 98 99 83 92 96 96 103 94	97 96 90 87 90 93 94 95 81	72 38 11 79 11 6 2 9 -66	-38 -79 -71 -74 -75 -75 -87 -67 -69	2.64E-6 1.03E-6 5.30E-7 2.57E-6 5.37E-7 5.23E-7 2.02E-6 5.59E-7 2.71E-7	7.52E-6 3.51E-6 2.25E-6 5.46E-6 2.26E-6 1.97E-6 4.37E-6 2.22E-6 5.92E-7	> 1.67E-5 9.36E-6 9.18E-6 1.16E-5 8.54E-6 8.13E-6 9.46E-6 1.00E-5 1.29E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.482 0.664 0.329 0.237 0.374 0.429 0.230	1.542 2.151 2.863 1.485 2.259 2.524 1.947	1.549 2.122 2.874 1.423 2.168 2.488 1.934	1.564 2.165 2.835 1.389 2.207 2.504 1.994	1.577 2.351 2.453 1.220 2.180 2.296 1.484	0.486 0.837 0.092 0.237 0.289 0.352 0.209	0.075 0.116 0.030 0.037 0.073 0.106 0.098	101 98 100 95 95 98 99	102 101 99 92 97 99 103	103 113 84 79 96 89 73	12 -72 -23 -18 -9	-85 -83 -91 -85 -80 -75 -57	5.50E-7 7.01E-7 2.75E-7 3.87E-7 4.06E-7 3.87E-7 3.87E-7 3.18E-7	1.69E-6 2.22E-6 5.76E-7 1.67E-6 1.07E-6 1.14E-6 1.29E-6	6.55E-6 7.53E-6 1.21E-6 6.51E-6 4.94E-6 6.05E-6 1.17E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.431 0.834 0.954 0.499 0.861 0.301	1.734 2.617 2.543 1.756 1.613 1.529	1.703 2.579 2.542 1.746 1.525 1.501	1.683 2.586 2.548 1.739 1.523 1.472	1.545 2.534 2.583 1.695 1.470 1.224	0.583 2.091 1.374 0.942 1.287 0.282	0.139 0.340 0.246 0.083 0.254 0.016	98 98 100 99 88 98	96 98 100 99 88 95	86 95 102 95 81 75	12 70 26 35 57 -6	-68 -59 -74 -83 -71 -95	5.06E-7 2.40E-6 8.18E-7 9.46E-7 1.88E-6 3.39E-7	2.34E-6 5.83E-6 3.05E-6 3.31E-6 4.66E-6 1.39E-6	9.96E-6 1.42E-5 9.59E-6 8.72E-6 1.15E-5 5.19E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-5 UACC-62	0.426 0.729 0.602 0.472 0.964 0.780 0.839 0.703	2.654 1.351 2.750 2.446 1.799 2.177 2.836 2.427	2.572 1.326 2.662 2.369 1.841 2.250 2.800 2.225	2.528 1.265 2.677 2.376 1.815 2.174 2.755 2.203	2.226 1.347 2.526 2.251 1.782 2.076 2.668 1.991	0.073 0.619 1.018 0.404 1.212 0.696 0.889 0.398	0.051 0.294 0.346 0.077 0.365 0.134 0.073 0.154	96 96 96 105 105 98 88	94 86 97 96 102 100 96 87	81 99 90 98 93 92 75	-83 -15 19 -14 30 -11 2 -43	-88 -60 -43 -84 -62 -83 -91 -78	2.58E-7 4.51E-7 6.11E-7 4.04E-7 8.42E-7 4.32E-7 4.89E-7 2.70E-7	5.21E-7 1.23E-6 3.43E-6 1.22E-6 3.52E-6 1.31E-6 1.77E-6 7.17E-7	1.05E-6 1.01E-5 5.45E-6 1.23E-5 5.85E-6 6.05E-6 2.59E-6
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.829 0.442 0.661 0.754 0.496 0.560 0.802	2.170 1.541 1.487 2.088 2.110 1.793 1.460	2.176 1.534 1.472 2.073 2.123 1.786 1.493	2.167 1.579 1.400 2.041 2.085 1.793 1.477	2.188 1.481 1.268 2.055 1.949 1.725 1.557	1.225 0.496 0.964 1.087 0.317 0.712 1.404	0.263 0.036 0.050 0.233 0.225 0.536 0.799	100 99 98 99 101 99 105	100 103 89 96 98 100 103	101 95 73 98 90 94 115	30 5 37 25 -36 12 91	-68 -92 -92 -69 -55 -4	8.67E-7 5.25E-7 7.23E-7 7.54E-7 3.47E-7 5.81E-7 4.72E-6	3.35E-6 1.88E-6 3.21E-6 3.07E-6 8.64E-7 9.14E-6 1.65E-5	1.08E-5 6.16E-6 7.83E-6 1.04E-5 9.39E-6 > 1.67E-5 > 1.67E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.605 1.169 0.483 0.592 0.963 0.648 0.762 0.811	2.530 2.057 1.992 2.133 1.682 2.113 1.610 2.129	2.455 1.969 2.011 1.994 1.667 2.055 1.537 1.985	2.504 1.973 2.061 2.025 1.640 2.037 1.566 1.949	2.452 2.055 2.001 2.036 1.617 1.985 1.628 1.996	0.587 1.949 0.281 0.679 1.255 0.582 1.041 0.719	0.039 0.891 0.053 0.015 0.174 0.254 0.077 0.105	96 90 101 91 98 96 91 89	99 90 105 93 94 95 95 86	96 100 101 94 91 91 102 90	-3 88 -42 6 41 -10 33 -11	-94 -24 -89 -98 -82 -61 -90 -87	4.86E-7 3.65E-6 3.78E-7 5.23E-7 1.09E-6 4.26E-7 9.46E-7 9.46E-7 4.13E-7	1.56E-6 1.02E-5 8.49E-7 1.89E-6 3.58E-6 1.33E-6 3.09E-6 1.29E-6	5.51E-6 > 1.67E-5 2.49E-6 5.78E-6 9.16E-6 1.02E-5 7.90E-6 5.41E-6
Prostate Cancer PC-3 DU-145	0.649 0.284	2.629 1.464	2.634 1.488	2.537 1.435	2.444 1.348	0.863 0.580	0.234 0.013	100 102	95 98	91 90	11 25	-64 -95	5.39E-7 6.92E-7	2.33E-6 2.70E-6	1.09E-5 7.01E-6
Breast Cancer MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.405 C 0.619 1.054 1.183 0.750 0.794	2.289 1.723 2.117 2.295 1.609 1.691	2.169 1.691 2.009 2.204 1.551 1.612	2.072 1.701 2.072 2.211 1.508 1.606	1.383 1.767 1.993 2.095 1.519 1.503	0.579 0.819 1.283 0.935 1.079 1.003	0.216 0.264 0.908 0.135 0.350 0.274	94 97 90 92 93 91	88 98 96 92 88 91	52 104 88 82 90 79	9 18 21 -21 38 23	-47 -57 -14 -89 -53 -65	1.85E-7 7.10E-7 6.26E-7 3.41E-7 9.85E-7 5.54E-7	2.44E-6 2.90E-6 6.76E-6 1.04E-6 4.37E-6 3.06E-6	> 1.67E-5 1.33E-5 > 1.67E-5 4.49E-6 1.53E-5 1.12E-5

		Natio	onal	Cano	er Ir	nstitu In-	ite Do Vitro	evelop Testii	men ng R	tal T esult	hera s	peutio	cs Prograr	n	
NSC : D - 786	055 / 1				Exp	erimer	nt ID:1	509NS56	5			Test	Гуре : 08	Units : N	lolar
Report Date :	Decemb	ber 27, 2	2015		Tes	t Date	: Septe	ember 08,	2015			QNS	:	MC :	
COMI : KCN-F	PGJ-47				Sta	in Rea	gent : S	RB Dual	Pass F	Related	1	SSPL	: 0ZAS		
						Lo	og10 Cor	ncentration	_						
Panel/Cell Line Leukemia	Time Zero	Ctrl	-8.6	Mear -7.6	1 Optica -6.6	I Densiti -5.6	es -4.6	-8.6	-7.6	ercent G -6.6	Frowth -5.6	-4.6	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.854 0.734 0.259 0.951 0.482 0.285	3.396 3.191 2.643 3.373 1.933 0.846	3.391 3.112 2.635 3.376 1.854 0.848	3.379 3.101 2.510 3.333 1.829 0.793	1.726 2.545 0.699 2.338 0.624 0.318	0.873 0.749 0.357 0.919 0.369 0.313	0.588 0.610 0.162 0.597 0.325 0.251	100 97 100 100 95 100	99 96 94 98 93 91	34 74 18 57 10 6	1 4 -3 -23 5	-31 -17 -38 -37 -33 -12	1.43E-7 5.27E-7 9.61E-8 3.29E-7 8.19E-8 7.53E-8	2.64E-6 2.70E-6 3.14E-6 2.20E-6 4.92E-7 4.93E-6	 > 2.50E-5
Non-Small Cell Lung A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H228 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.397 0.829 0.551 1.496 0.568 0.617 0.662 0.217 0.922	1.940 2.149 1.535 2.011 1.497 1.866 1.955 2.583 2.411	1.866 2.052 1.508 1.913 1.436 1.825 1.822 2.587 2.339	1.827 2.024 1.518 1.881 1.417 1.712 1.863 2.483 2.208	1.820 2.019 1.379 1.906 1.348 1.632 1.750 2.141 1.527	0.452 0.975 0.372 1.212 0.445 0.389 0.738 0.738 0.193 0.219	0.068 0.577 0.172 0.325 0.185 0.146 0.049 0.073 0.114	95 93 97 81 93 97 90 100 95	93 91 98 75 91 88 93 96 86	92 90 84 80 84 81 84 81 41	4 -33 -19 -22 -37 6 -11 -76	-83 -30 -69 -78 -68 -76 -93 -66 -88	7.48E-7 8.05E-7 4.90E-7 5.24E-7 4.59E-7 6.83E-7 5.45E-7 1.56E-7	2.75E-6 4.62E-6 1.31E-6 1.60E-6 1.56E-6 1.52E-6 2.87E-6 1.89E-6 5.56E-7	1.04E-5 > 2.50E-5 7.55E-6 8.34E-6 1.04E-5 5.34E-6 9.22E-6 1.26E-5 1.49E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.482 0.664 0.329 0.237 0.374 0.429 0.230	1.488 2.276 2.969 1.433 2.223 2.671 2.094	1.550 2.180 2.861 1.397 2.225 2.580 2.083	1.532 2.189 2.867 1.252 2.209 2.514 2.037	1.422 2.176 1.534 0.602 1.573 2.098 0.579	0.161 0.088 0.199 0.152 0.132 0.243 0.243	0.066 0.126 0.053 0.041 0.085 0.097 0.064	106 94 96 97 100 96 99	104 95 96 85 99 93 97	93 94 46 30 65 74 19	-67 -87 -40 -36 -65 -43 -31	-86 -81 -84 -83 -77 -77 -72	4.67E-7 4.37E-7 2.05E-7 1.09E-7 3.25E-7 4.03E-7 9.95E-8	9.58E-7 8.26E-7 8.59E-7 7.20E-7 7.90E-7 1.07E-6 5.96E-7	1.97E-6 1.56E-6 4.30E-6 5.01E-6 1.92E-6 3.89E-6 7.22E-6
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.431 0.834 0.954 0.499 0.861 0.301	1.756 2.583 2.681 1.868 1.706 1.453	1.718 2.502 2.565 1.831 1.558 1.439	1.566 2.487 2.509 1.832 1.523 1.428	1.383 2.487 2.457 1.556 1.496 0.837	0.425 0.798 0.681 0.680 1.184 0.126	0.215 0.251 0.201 0.131 0.205 0.025	97 95 93 97 82 99	86 94 90 97 78 98	72 94 87 77 75 47	-1 -4 -29 13 38 -58	-50 -70 -79 -74 -76 -92	4.96E-7 7.05E-7 5.23E-7 6.65E-7 1.19E-6 2.14E-7	2.39E-6 2.26E-6 1.41E-6 3.54E-6 5.39E-6 6.94E-7	2.47E-5 1.24E-5 6.65E-6 1.33E-5 1.48E-5 2.08E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-62	0.426 0.729 0.602 0.472 0.964 0.780 0.839 0.703	2.739 1.396 2.763 2.541 1.817 2.251 2.869 2.667	2.648 1.322 2.709 2.454 1.830 2.215 2.780 2.487	2.500 1.328 2.673 2.384 1.755 2.181 2.684 2.499	1.357 1.200 2.401 1.328 1.667 2.006 2.466 1.763	0.058 0.497 0.750 0.409 0.547 0.449 0.117 0.524	0.040 0.239 0.187 0.087 0.168 0.048 0.031 0.170	96 89 98 96 101 98 96 91	90 90 92 93 95 91 91	40 71 83 41 82 83 80 54	-86 -32 -13 -43 -43 -86 -25	-91 -67 -82 -83 -94 -96 -76	1.59E-7 3.98E-7 6.81E-7 1.69E-7 4.53E-7 4.60E-7 3.80E-7 2.80E-7	5.20E-7 1.22E-6 3.08E-6 1.43E-6 1.13E-6 1.15E-6 7.59E-7 1.19E-6	1.29E-6 8.14E-6 1.40E-5 8.61E-6 3.71E-6 3.50E-6 1.52E-6 7.67E-6
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.829 0.442 0.661 0.754 0.496 0.560 0.802	2.263 1.698 1.459 2.078 2.150 1.871 1.430	2.136 1.673 1.455 1.985 2.184 1.814 1.408	2.202 1.609 1.369 2.022 2.057 1.769 1.426	2.091 0.923 1.267 1.919 1.089 1.415 1.458	0.739 0.220 0.911 0.652 0.529 0.552 0.906	0.371 0.023 0.160 0.325 0.183 0.527 0.016	91 98 100 93 102 96 96	96 93 89 96 94 92 99	88 38 76 88 36 65 104	-11 -50 31 -14 2 -2 17	-55 -95 -76 -57 -63 -6 -98	6.05E-7 1.53E-7 9.52E-7 5.92E-7 1.43E-7 4.23E-7 1.04E-6	1.94E-6 6.77E-7 4.90E-6 1.84E-6 2.68E-6 2.37E-6 3.49E-6	1.90E-5 2.49E-6 1.43E-5 1.73E-5 1.57E-5 > 2.50E-5 9.52E-6
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.605 1.169 0.483 0.592 0.963 0.648 0.762 0.811	2.358 2.126 2.025 2.295 1.628 2.453 1.688 2.254	2.271 2.040 2.089 2.140 1.573 2.351 1.626 1.997	2.303 2.170 2.036 2.176 1.539 2.372 1.649 2.069	2.260 2.059 1.398 1.857 1.521 2.057 1.695 1.888	0.335 0.821 0.202 0.469 0.176 0.658 0.507 0.069	0.124 0.030 0.037 0.178 0.377 0.024 0.053	95 91 104 91 92 94 93 82	97 105 101 93 87 95 96 87	94 93 59 74 84 78 101 75	-45 -30 -58 -21 -82 1 -34 -91	-80 -91 -94 -82 -42 -97 -94	5.21E-7 5.60E-7 3.00E-7 4.50E-7 4.00E-7 5.75E-7 5.97E-7 3.52E-7	1.19E-6 1.43E-6 8.00E-7 1.51E-6 8.02E-7 2.57E-6 1.41E-6 7.03E-7	3.56E-6 5.33E-6 2.13E-6 6.29E-6 1.61E-6 > 2.50E-5 4.55E-6 1.41E-6
Prostate Cancer PC-3 DU-145	0.649 0.284	2.681 1.483	2.642 1.519	2.534 1.465	1.980 1.225	0.361 0.251	0.099 0.012	98 103	93 99	65 79	-44 -12	-85 -96	3.46E-7 5.17E-7	9.86E-7 1.85E-6	3.45E-6 7.11E-6
Breast Cancer MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.405 C 0.619 1.054 1.183 0.750 0.794	2.275 1.802 2.149 2.234 1.513 1.664	2.164 1.794 2.085 2.204 1.461 1.571	2.002 1.819 2.059 2.244 1.450 1.516	0.740 1.607 1.913 2.171 1.361 1.319	0.420 0.759 1.214 0.674 0.735 0.388	0.244 0.417 1.081 0.271 0.437 0.245	94 99 94 97 93 89	85 101 92 101 92 83	18 83 78 94 80 60	1 12 15 -43 -2 -51	-40 -33 2 -77 -42 -69	8.36E-8 7.33E-7 6.98E-7 5.24E-7 5.80E-7 3.09E-7	2.61E-6 4.61E-6 > 2.50E-5 1.21E-6 2.36E-6 8.69E-7	 > 2.50E-5 > 2.50E-5 > 2.50E-5 4.00E-6 > 2.50E-5 2.44E-6

Developmental Ther	apeutics Program	NSC: D-786060 / 1	Conc: 1.00E-5 Molar	Test Date: Aug 10, 2015
One Dose Mea	an Graph	Experiment ID: 1508	OS37	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Per	cent
Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer	103.48 99.87 104.75 100.12 107.19 102.38		-	
A349/A100 EKVX HOP-62 HOP-92 NCI-H226 NCI-H23 NCI-H322M NCI-H460 NCI-H522	98.80 100.75 88.37 109.58 103.29 91.23 94.18 111.68 84.25		È	
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer	100.95 88.92 96.38 101.00 94.03 106.20 107.67			
SF-268 SF-295 SF-539 SNB-19 SNB-75 U251 Melanoma U251	96.29 97.91 99.29 111.23 91.96 102.53		-	
MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-62 Ovaria Cancer	92.03 95.84 102.41 106.60 99.99 112.37 105.21 109.50		1	
IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3 Renal Cancer	113.82 109.44 112.72 93.48 104.42 96.99 90.03			
786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31 Prostate Cancer	94.21 82.33 108.88 100.56 117.00 106.50 84.30 91.07			
PC-3 DU-145 Breast Cancer MCF7 MDA-MB-231/ATCC HS 578T	93.40 108.94 92.49 104.56 110.17			
BT-549 T-47D MDA-MB-468	103.73 83.50 99.11			
Mean Delta Range	100.34 18.01 34.67			
	150	100 50	0 -50	-100 -150

Developmental Ther	apeutics Program	NSC: D-786061/1	Conc: 1.00E-5 Molar	Test Date: Aug 10, 2015
One Dose Mea	an Graph	Experiment ID: 1508	OS37	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Per	cent
Panel/Cell Line Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer A549/ATCC EKVX HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H32 SWC-B2 Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer SF-268 SF-295 SF-393 SNB-75 U251 Melanoma	Growth Percent 91.71 70.55 82.61 82.14 94.31 85.52 79.43 90.78 79.16 103.47 92.17 77.14 92.72 103.73 56.22 103.26 104.61 87.18 93.29 86.45 97.42 111.97 95.42 102.55 104.70 114.00 86.36 101.04 91.46 84.60 98.80 102.84 93.83 115.50 86.27	Mean Growth	Percent - Growth Per	cent
UACC-62 Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-0V-3 Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31 Prostate Cancer PC-3 DU-145 Breast Cancer MCF7 MDA-MB-231/ATCC HS 578T BT-549 T-47D MDA-MB-468 Mean Delta Range	91.30 89.97 99.81 84.83 106.53 97.21 92.76 93.54 99.31 101.42 109.79 87.17 107.94 107.50 79.44 78.12 90.90 100.86 87.35 102.88 104.76 109.46 62.21 71.67 93.22 37.00 59.28	100 50		-100 -150
	150	100 50	0 -50	-100 -150

		Natio	onal	Cano	er Ir	nstitu In-	ite Do Vitro	evelop Testir	mer ng R	ital T esult	hera s	peutio	cs Progra	m	
NSC : D - 782	784 / 1				Exp	erimer	nt ID:1	501NS12	2			Test	Гуре : 08	Units : N	Iolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Janua	ary 05, 20	15			QNS	:	MC :	
COMI : KCN-F	PGJ-26				Sta	in Rea	gent : S	RB Dual	Pass	Related	1	SSPL	: 0ZAS		
	_					L	og10 Cor	ncentration							
Panel/Cell Line	Zero	Ctrl	-8.5	Mear -7.5	-6.5	-5.5	es -4.5	-8.5	-7.5	ercent G -6.5	-5.5	-4.5	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.496 0.691 0.237 0.509 0.852 0.305	2.324 2.614 2.228 2.395 2.354 1.700	2.215 2.599 1.942 2.410 2.301 1.619	2.207 2.684 1.977 2.379 2.349 1.568	2.188 2.590 1.992 2.230 2.417 1.562	0.666 1.682 1.074 0.801 0.998 0.452	0.456 0.549 0.362 0.449 0.850 0.249	94 99 86 101 96 94	94 104 87 99 100 91	93 99 88 91 104 90	9 52 42 15 10 11	-8 -21 6 -12 -19	1.05E-6 3.41E-6 2.18E-6 1.14E-6 1.22E-6 1.04E-6	1.11E-5 1.68E-5 > 3.25E-5 1.20E-5 3.08E-5 7.49E-6	> 3.25E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5
Non-Small Cell Lung A549/ATCC EKVX HOP-62 NCI-H226 NCI-H23 NCI-H322M NCI-H322M NCI-H460 NCI-H522	Cancer 0.370 0.671 0.818 1.554 0.697 0.786 0.354 1.013	1.995 1.818 1.943 2.511 2.164 1.868 3.177 2.358	1.881 1.801 1.894 2.268 2.089 1.792 3.150 2.280	1.986 1.626 1.836 2.467 2.069 1.864 3.177 2.316	1.986 1.713 2.005 2.428 2.123 1.857 3.243 2.215	1.875 1.651 2.082 2.579 2.020 1.832 3.014 1.951	0.264 0.598 0.366 1.166 0.538 0.688 0.347 0.378	93 99 96 75 93 99 94	99 83 91 95 94 100 100 97	99 91 106 91 97 99 102 89	93 85 112 107 90 97 94 70	-29 -11 -55 -25 -23 -12 -2 -2 -63	7.30E-6 7.59E-6 8.80E-6 7.36E-6 8.69E-6 9.35E-6 4.58E-6	1.88E-5 2.51E-5 2.10E-5 2.10E-5 2.04E-5 2.50E-5 3.09E-5 1.09E-5	 > 3.25E-5 > 2.60E-5
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.375 0.850 0.219 0.372 0.210 0.488 0.344	1.433 2.708 1.922 2.273 1.441 2.989 2.489	1.462 2.658 2.010 2.228 1.461 2.996 2.446	1.399 2.862 1.998 2.163 1.504 3.036 2.496	1.535 2.889 2.076 2.185 1.607 2.910 2.670	1.215 3.016 0.442 1.587 1.131 2.167 1.862	0.155 0.122 0.077 0.231 0.131 0.279 0.289	103 97 105 98 102 100 98	97 108 104 94 105 102 100	110 110 109 95 113 97 108	79 117 13 64 75 67 71	-59 -86 -65 -38 -38 -43 -16	5.30E-6 6.93E-6 1.34E-6 4.45E-6 5.40E-6 4.65E-6 5.64E-6	1.22E-5 1.22E-5 4.78E-6 1.38E-5 1.50E-5 1.33E-5 2.13E-5	2.81E-5 2.16E-5 2.09E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.637 0.829 0.882 0.553 0.932 0.446	2.448 2.944 2.500 1.860 1.822 2.053	2.396 2.816 2.420 1.881 1.684 2.021	2.421 2.805 2.444 1.848 1.671 2.041	2.368 3.049 2.495 1.905 1.751 2.119	2.059 2.963 2.443 1.631 1.640 1.461	0.540 0.511 0.549 0.499 1.190 0.087	97 94 95 102 85 98	99 93 97 99 83 99	96 105 100 103 92 104	79 101 96 82 80 63	-15 -38 -38 -10 29 -80	6.55E-6 7.53E-6 7.21E-6 7.31E-6 1.25E-5 4.01E-6	2.24E-5 1.72E-5 1.70E-5 2.54E-5 > 3.25E-5 8.94E-6	> 3.25E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5 1.99E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	0.409 0.807 0.436 0.577 0.851 0.643 0.874 0.978 0.695	2.839 1.623 1.799 2.781 1.552 1.812 2.630 2.017 2.276	2.719 1.606 1.719 2.729 1.573 1.793 2.513 1.949 2.177	2.709 1.615 1.787 2.768 1.575 1.753 2.545 1.983 2.186	2.698 1.625 1.788 2.800 1.563 1.880 2.571 2.012 2.219	1.865 1.568 1.542 1.918 1.476 1.529 2.310 1.815 1.715	0.025 0.679 0.342 0.281 0.550 0.238 0.004 0.319 0.304	95 98 94 103 98 93 93 94	95 99 99 103 95 95 97 94	94 100 99 101 102 106 97 100 96	60 93 81 61 89 76 82 81 65	-94 -16 -22 -51 -35 -63 -100 -67 -56	3.77E-6 8.08E-6 6.53E-6 4.06E-6 6.70E-6 4.98E-6 4.86E-6 5.23E-6 4.29E-6	7.97E-6 2.32E-5 2.00E-5 1.13E-5 1.69E-5 9.18E-6 1.14E-5 1.14E-5 1.11E-5	1.68E-5 > 3.25E-5 3.16E-5 3.25E-5 2.62E-5 1.73E-5 2.48E-5 2.88E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.598 0.778 0.826 0.568 0.456 0.577 1.108	2.133 2.212 1.943 1.544 1.952 2.033 2.259	2.169 2.235 1.916 1.555 1.956 1.977 2.270	2.111 2.311 1.821 1.448 1.906 2.044 2.192	2.309 2.290 1.853 1.570 1.987 1.994 2.338	2.101 2.123 1.608 1.534 0.619 1.553 2.378	0.595 0.632 1.018 0.437 0.303 0.778 1.198	102 102 98 101 100 96 101	99 107 89 90 97 101 94	111 105 92 103 102 97 107	98 94 70 99 11 67 110	-19 17 -23 -34 14 8	9.97E-6 7.96E-6 7.76E-6 8.18E-6 1.21E-6 6.78E-6 1.26E-5	3.21E-5 2.21E-5 3.25E-5 2.10E-5 5.71E-6 > 3.25E-5 > 3.25E-5	 3.25E-5 3.25E-5 3.25E-5 3.25E-5 3.25E-5 3.25E-5 3.25E-5 3.25E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.713 1.498 0.591 0.685 1.265 0.521 0.883 0.771	2.291 2.513 1.983 3.179 1.778 1.524 1.877 2.724	2.194 2.275 1.988 3.171 1.743 1.497 1.803 2.605	2.277 2.215 1.985 3.049 1.767 1.528 1.808 2.657	2.466 2.283 2.160 3.166 1.765 1.601 1.945 2.657	2.534 2.413 1.725 2.634 1.700 1.381 2.198 2.485	0.195 0.300 0.073 0.583 0.173 0.410 0.790 0.284	94 77 100 100 93 97 93 94	99 71 100 95 98 100 93 97	111 77 113 99 97 108 107 97	115 90 81 78 85 86 132 88	-73 -80 -88 -15 -86 -21 -11 -63	7.24E-6 5.59E-6 4.99E-6 5.52E-6 5.19E-6 7.01E-6 1.22E-5 5.78E-6	1.33E-5 1.10E-5 9.85E-6 2.25E-5 1.02E-5 2.05E-5 2.74E-5 1.24E-5	2.46E-5 2.17E-5 1.95E-5 3.25E-5 1.92E-5 3.22E-5 3.25E-5 2.66E-5
Prostate Cancer PC-3 DU-145 Breast Cancer	0.585 0.448	2.125 2.207	2.069 2.276	2.116 2.282	2.299 2.167	1.868 1.896	0.359 0.448	96 104	99 104	111 98	83 82	-39	6.09E-6 8.02E-6	1.57E-5 3.24E-5	> 3.25E-5 > 3.25E-5
MDA-MB-231/ATC0 MDA-MB-231/ATC0 HS 578T BT-549 T-47D MDA-MB-468	0.329 0.605 1.110 0.925 0.740 1.040	1.922 1.513 2.279 1.998 1.540 1.728	1.762 1.505 2.205 1.974 1.471 1.639	1.717 1.534 2.219 2.011 1.461 1.781	1.733 1.625 2.328 2.072 1.496 1.701	0.738 1.562 2.193 1.924 1.348 1.437	0.356 0.714 1.364 0.318 0.644 0.546	90 99 94 98 91 87	87 102 95 101 90 108	88 112 104 107 95 96	26 105 93 93 76 58	2 12 22 -66 -13 -48	1.32E-6 1.27E-5 1.30E-5 6.07E-6 6.37E-6 3.85E-6	 > 3.25E-5 > 3.25E-5 > 3.25E-5 1.25E-5 2.32E-5 1.15E-5 	 > 3.25E-5 > 3.25E-5 > 3.25E-5 2.59E-5 > 3.25E-5 > 3.25E-5 > 3.25E-5

		Natio	onal	Cano	cer Ir	nstitu In-	ite De Vitro	evelop Testir	mer ng R	ital T esult	hera s	peuti	cs Program	1	
NSC : D - 782	2785 / 1				Exp	erimer	nt ID : 1	501NS12	2			Test	Туре : 08	Units : N	/lolar
Report Date :	Decem	ber 27, 2	2015		Tes	t Date	: Janua	ary 05, 20	15			QNS	:	MC :	
COMI : KCN-	PGJ-27				Sta	in Rea	gent : S	RB Dual	Pass I	Related	ł	SSPI	L:0ZAS		
	_					Lo	og10 Cor	ncentration							
Panel/Cell Line	Time Zero	Ctrl	-8.3	Mear -7.3	-6.3	-5.3	es -4.3	-8.3	P -7.3	ercent G -6.3	-5.3	-4.3	GI50	TGI	LC50
CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.496 0.691 0.237 0.509 0.852 0.305	2.261 2.651 2.022 2.356 2.365 1.745	2.354 2.653 2.126 2.373 2.423 1.651	2.348 2.609 2.007 2.319 2.451 1.627	2.037 2.526 1.893 2.215 2.201 1.488	0.547 0.752 0.285 0.520 0.866 0.256	0.276 0.497 0.175 0.378 0.665 0.234	105 100 106 101 104 94	105 98 99 98 106 92	87 94 93 92 89 82	3 3 1 1 -16	-44 -28 -26 -26 -22 -23	1.38E-6 1.52E-6 1.49E-6 1.45E-6 1.39E-6 1.06E-6	5.75E-6 6.29E-6 6.19E-6 5.27E-6 5.49E-6 3.42E-6	> 5.00E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5
Non-Small Cell Lun A549/ATCC EKVX HOP-62 NCI-H226 NCI-H23 NCI-H322M NCI-H322M NCI-H522	g Cancer 0.370 0.671 0.818 1.554 0.697 0.786 0.354 1.013	1.897 1.829 1.931 2.262 2.146 1.907 3.171 2.404	1.865 1.733 1.838 2.360 2.049 1.906 3.240 2.316	1.858 1.704 1.873 2.295 1.978 1.930 3.274 2.203	1.909 1.782 2.062 2.419 2.049 1.947 3.175 2.214	0.615 1.274 0.643 2.664 1.060 1.215 0.321 1.019	0.245 0.100 0.234 1.428 0.359 0.145 0.121 0.398	98 92 114 93 100 102 94	97 89 95 105 88 102 104 86	101 96 112 122 93 104 100 86	16 52 -21 157 25 38 -9	-34 -85 -71 -8 -49 -82 -66 -61	1.99E-6 5.17E-6 1.45E-6 2.22E-5 2.16E-6 3.30E-6 1.44E-6 1.32E-6	1.05E-5 1.20E-5 3.45E-6 4.46E-5 1.09E-5 1.04E-5 4.11E-6 5.08E-6	 > 5.00E-5 2.77E-5 1.87E-5 > 5.00E-5 > 5.00E-5 2.72E-5 2.61E-5 3.34E-5
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	0.375 0.850 0.219 0.372 0.210 0.488 0.344	1.398 2.597 2.045 2.234 1.433 2.825 2.464	1.402 2.616 2.154 2.029 1.406 2.828 2.435	1.454 2.541 2.142 1.979 1.465 2.838 2.461	1.458 2.774 1.856 1.923 1.556 2.737 2.564	0.232 1.625 0.062 0.355 0.203 0.397 0.335	0.059 0.079 0.003 0.055 0.088 0.071 0.066	100 101 106 89 98 100 99	105 97 105 86 103 101 100	106 110 90 83 110 96 105	-38 44 -72 -5 -3 -19 -3	-84 -91 -85 -58 -86 -81	1.22E-6 4.10E-6 8.80E-7 1.19E-6 1.69E-6 1.26E-6 1.62E-6	2.72E-6 1.06E-5 1.79E-6 4.42E-6 4.67E-6 3.43E-6 4.73E-6	9.04E-6 2.50E-5 3.66E-6 1.83E-5 3.53E-5 1.47E-5 2.01E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.637 0.829 0.882 0.553 0.932 0.446	2.355 3.002 2.657 1.836 1.914 2.096	2.256 2.721 2.448 1.849 1.691 2.137	2.218 2.851 2.632 1.830 1.771 2.100	2.258 2.962 2.633 1.831 1.781 2.077	0.925 1.356 1.705 0.884 1.505 0.665	0.079 0.118 0.122 0.161 -0.004 0.006	94 87 88 101 77 102	92 93 99 100 85 100	94 98 99 100 86 99	17 24 46 26 58 13	-88 -86 -86 -71 -100 -99	1.86E-6 2.24E-6 4.26E-6 2.35E-6 5.64E-6 1.86E-6	7.23E-6 8.30E-6 1.12E-5 9.23E-6 1.17E-5 6.57E-6	2.18E-5 2.36E-5 2.67E-5 3.03E-5 2.42E-5 1.84E-5
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.409 0.807 0.436 0.577 0.851 0.643 0.874 0.978 0.695	2.705 1.663 1.803 2.886 1.573 1.991 2.504 2.013 2.251	2.614 1.643 1.794 2.806 1.546 1.858 2.524 2.008 2.156	2.538 1.636 1.841 2.861 1.545 1.929 2.447 2.034 2.205	2.412 1.632 1.786 2.804 1.550 1.954 2.555 1.979 2.099	0.111 0.981 0.504 0.462 1.209 0.640 0.644 1.327 0.316	0.028 0.290 0.122 0.095 0.257 0.089 -0.015 0.231 0.153	96 98 99 97 96 90 101 99 94	93 97 103 99 96 95 97 102 97	87 96 99 97 97 103 97 90	-73 20 5 -20 50 -26 34 -55	-93 -64 -72 -84 -70 -86 -100 -76 -78	8.54E-7 2.03E-6 1.65E-6 4.88E-6 1.52E-6 1.52E-6 1.29E-6 2.76E-6 9.48E-7	1.75E-6 8.70E-6 3.37E-6 1.30E-5 4.94E-6 3.13E-6 1.01E-5 2.10E-6	3.60E-6 3.40E-5 2.59E-5 1.48E-5 3.41E-5 1.89E-5 1.05E-5 2.88E-5 4.65E-6
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.598 0.778 0.826 0.568 0.456 0.577 1.108	2.240 2.174 1.832 1.627 1.937 1.997 2.177	2.312 2.190 1.789 1.575 1.924 1.949 2.107	2.207 2.162 1.839 1.633 2.053 1.920 2.177	2.210 2.229 1.794 1.764 2.021 1.997 2.242	0.865 0.999 1.231 0.958 0.675 0.671 2.000	0.282 0.020 0.066 0.246 0.350 0.570 0.889	104 101 95 99 97 93	98 99 101 101 108 95 100	98 104 96 113 106 100 106	16 16 40 37 15 7 83	-53 -97 -92 -57 -23 -1 -20	1.94E-6 2.05E-6 3.35E-6 3.35E-6 2.05E-6 1.71E-6 1.05E-5	8.58E-6 6.90E-6 1.01E-5 1.24E-5 1.22E-5 3.50E-5 3.21E-5	4.54E-5 1.91E-5 2.40E-5 4.23E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5 > 5.00E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.713 1.498 0.591 0.685 1.265 0.521 0.883 0.771	2.334 2.462 2.163 3.171 1.677 1.520 1.857 2.763	2.366 2.439 2.081 3.046 1.731 1.499 1.809 2.670	2.416 2.355 2.170 3.082 1.691 1.486 1.788 2.671	2.546 2.352 2.170 3.119 1.772 1.498 2.001 2.686	1.104 2.486 1.024 1.041 1.565 0.403 1.575 1.227	0.274 0.175 0.125 0.057 0.172 0.167 0.284 0.336	102 98 95 113 98 95 95	105 89 100 96 103 97 93 95	113 89 100 98 123 98 115 96	24 102 28 14 73 -23 71 23	-62 -88 -79 -92 -86 -68 -68 -56	2.56E-6 9.41E-6 2.46E-6 1.87E-6 6.95E-6 1.25E-6 7.09E-6 2.13E-6	9.55E-6 1.72E-5 9.07E-6 6.82E-6 1.43E-5 3.24E-6 1.62E-5 9.72E-6	3.66E-5 3.15E-5 2.68E-5 2.02E-5 2.95E-5 2.00E-5 3.72E-5 4.15E-5
Prostate Cancer PC-3 DU-145	0.585 0.448	2.147 2.137	2.107 2.141	2.162 2.096	2.212 2.091	0.653 1.096	0.164 0.033	97 100	101 98	104 97	4 38	-72 -93	1.74E-6 3.17E-6	5.70E-6 9.81E-6	2.58E-5 2.36E-5
Breast Cancer MCF7 MDA-MB-231/ATC HS 578T BT-549 T-47D MDA-MB-468	0.329 C 0.605 1.110 0.925 0.740 1.040	1.970 1.502 2.285 2.013 1.556 1.585	1.702 1.523 2.265 2.039 1.482 1.710	1.782 1.528 2.302 2.023 1.493 1.594	1.442 1.578 2.285 2.059 1.465 1.705	0.502 0.678 1.591 0.840 0.766 1.324	0.132 0.267 0.835 0.100 0.259 0.570	84 102 98 102 91 123	89 103 101 101 92 102	68 108 100 104 89 122	11 8 41 -9 3 52	-60 -56 -25 -89 -65 -45	1.02E-6 1.91E-6 3.51E-6 1.50E-6 1.42E-6 5.26E-6	7.05E-6 6.70E-6 2.10E-5 4.15E-6 5.57E-6 1.72E-5	3.60E-5 4.04E-5 > 5.00E-5 1.62E-5 3.01E-5 > 5.00E-5

Developmental Ther	apeutics Program	NSC: D-782130 / 1	Conc: 1.00E-5 Molar	Test Date: Sep 29, 2014
One Dose Mea	an Graph	Experiment ID: 1409	OS61	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Per	cent
Panel/Cell Line Leukemia HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H322M NCI-H322 Colon Cancer COLO 205 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer SF-268 SF-295 SF-539 SNB-175 U251 Melanoma LOX IMVI MALME-3M	Growth Percent 96.69 89.23 96.50 103.13 88.61 85.01 106.14 103.13 124.41 107.95 104.39 97.59 101.03 80.65 107.59 97.22 98.92 107.65 97.76 100.73 107.03 98.91 106.52 108.65 98.74 94.22 88.93 102.55 97.63 104.30	Mean Growth	Percent - Growth Perc	cent
MIALME-301 M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-28 UACC-257 UACC-62 Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-4 OVCAR-5 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3 Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31 Prostate Cancer PC-3 DU-145 Breast Cancer MCF7 MDA-MB-231/ATCC HS 578T BT-549 T-47D MDA-MB-231/ATCC HS 578T BT-549 T-47D MDA-MB-468 Mean Delta Range	97.63 104.30 108.43 101.50 112.74 90.66 91.53 94.75 102.36 110.61 105.53 108.44 102.92 105.23 106.67 107.28 92.65 109.95 103.07 100.37 103.77 98.79 100.37 107.78 97.81 86.15 107.09 100.31 106.91 89.92 110.76 100.96 101.61 100.98 20.33 43.76			
	150	100 50	0 -50	 J -100 -150
Developmental Ther	apeutics Program	NSC: D-782131 / 1	Conc: 1.00E-5 Molar	Test Date: Sep 29, 2014
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One Dose Mea	an Graph	Experiment ID: 1409	OS61	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Per	cent
Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR Non-Small Cell Lung Cancer	83.71 97.03 94.30 91.95 100.68 83.70			
A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H23 NCI-H322M NCI-H322M NCI-H522	88.70 106.99 112.94 109.44 98.92 99.11 94.60 106.29 80.45		1	
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620 CNS Cancer	115.95 121.61 102.76 95.41 107.51 104.91 104.66			
SF-268 SF-295 SF-539 SNB-19 SNB-75 U251 Melanoma	98.38 103.67 106.88 99.72 91.30 92.23		Ę	
MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-257 UACC-62 Ovaria Cancer	114.07 101.44 113.18 97.35 122.57 97.58 80.77 92.76			
IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-5 NCI/ADR-RES SK-OV-3 Renal Cancer	109.23 108.60 102.03 123.53 94.05 105.98 115.15			
785-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31 Prostate Cancer	84.54 106.05 109.37 112.89 96.19 112.51 91.68			
PC-3 DU-145 Breast Cancer MCF7 MDA-MB-231/ATCC HS 578T BT-549 T-47D MDA-MB-468	93.81 103.81 92.84 100.15 90.51 104.32 90.93 92.59			
Mean Delta Range	100.84 20.39 43.08			
	150	100 50	0 -50	-100 -150

Developmental Ther	apeutics Program	NSC: D-782790 / 1	Conc: 1.00E-5 Molar	Test Date: Dec 08, 2014
One Dose Mea	an Graph	Experiment ID: 1412	2OS02	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Per	cent
$\begin{tabular}{lllllllllllllllllllllllllllllllllll$	91.02 102.29 88.30 106.36 81.74 73.61 104.38 94.25 98.79 91.69 101.86 105.08 101.44 114.50 96.38 98.32 78.38 104.70 111.26 101.69 100.03 94.65 111.47 83.97 97.29 111.89 99.04 103.32 65.69 113.34 97.03 75.06 90.40 109.63 110.12 116.42	Mean Growth	Percent - Growth Per	
OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3 Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31 Prostate Cancer PC-3 DU-145 Breast Cancer MCF7 MDA-MB-231/ATCC HS 578T BT-549 T-47D MDA-MB-468 Mean Delta Range	116.42 112.77 89.25 105.89 94.66 112.82 100.12 99.81 102.98 106.92 80.13 99.17 88.00 89.96 115.89 84.81 95.06 98.15 100.77 67.13 85.82 96.77 47.29 66.94	100 50	0 -50	-100 -150

Developmental Ther	apeutics Program	NSC: D-782791/1	Conc: 1.00E-5 Molar	Test Date: Dec 08, 2014
One Dose Mea	an Graph	Experiment ID: 1412	OS02	Report Date: Dec 27, 2015
Panel/Cell Line	Growth Percent	Mean Growth	Percent - Growth Perc	cent
Leukemia CCRF-CEM K-562 MOLT-4 RPMI-8226 SR	94.37 110.36 102.97 109.34 89.18		3	
Non-Small Cell Lung Cancer	69.24 108.36 73.58 95.33 85.78 101.91 100.57 98.07 54.95		Ē	
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 KM12 SW-620	105.39 103.96 98.37 98.25 72.18 102.50 92.02		1	
CNS Cancer SF-268 SF-295 SNB-19 SNB-75 U251 Melanoma L OX IMVI	103.75 101.26 95.17 92.23 86.91 96.82		1	
MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62 Ovarian Cancer	110.47 101.67 91.33 82.88 104.86 99.23 69.81 94.63			
IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3 Renal Cancer	98.49 108.02 108.33 101.67 85.98 108.87 79.89			
786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31 Prostate Cancer	110.46 74.37 97.42 97.22 102.27 91.17 93.45 84.89			
PC-3 DU-145 Breast Cancer MCF7 MDA-MB-231/ATCC HS 578T BT-549 T-47D MDA-MB-468	84.52 115.34 91.19 99.75 87.56 99.83 68.32 94.53			
Mean Delta Range	94.50 39.55 60.39			
	150	100 50	0 -50	-100 -150

		Natio	onal	Cano	er Ir	nstitu In-	ite D Vitro	evelop Testi	omen ng R	ital T esult	hera s	peuti	cs Progran	n	
NSC : D - 788	3111 / 1				Exp	erimer	nt ID : 1	512NS26	6			Test	Type : 08	Units : N	Iolar
Report Date :	Februa	ry 08, 20	016		Tes	t Date	: Dece	mber 20,	2015			QNS	:	MC :	
COMI : KCN-	PGJ-59				Sta	in Rea	gent : S	RB Dual	-Pass I	Related		SSPL	: 0ZAS		
Panel/Coll Line	Time	Ctrl	0.2	Mear	n Optica	Lo Densiti	og10 Col	ncentration	P	ercent G	F 2	4.3	CI50	TGI	1 0 50
Leukemia CCRF-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	0.564 1.034 0.258 0.567 0.864 0.327	2.483 2.764 1.788 2.207 2.441 1.591	2.296 2.644 1.829 2.160 2.408 1.610	1.978 2.614 1.570 2.008 2.238 1.330	0.592 0.849 0.316 0.648 0.747 0.390	0.564 0.876 0.290 0.510 0.677 0.339	0.478 0.708 0.255 0.456 0.528 0.346	90 93 103 97 98 102	74 91 86 88 87 79	-0.5 -18 -18 5 -14 5	-15 2 -10 -22 1	-15 -32 -1 -20 -39 2	1.06E-7 1.20E-7 1.36E-7 1.43E-7 1.17E-7 1.24E-7	5.00E-6 3.43E-7 2.20E-5 1.06E-6 3.66E-7 > 5.00E-5	 5.00E-5 5.00E-5 5.00E-5 5.00E-5 5.00E-5 5.00E-5 5.00E-5
Non-Small Cell Lun A549/ATCC EKVX HOP-62 HOP-92 NCI-H226 NCI-H226 NCI-H227 NCI-H322M NCI-H460 NCI-H522	g Cancer 0.329 0.709 0.869 1.598 1.106 0.631 0.715 0.243 1.165	1.313 2.115 1.854 2.035 2.578 1.987 2.083 2.696 1.783	1.249 2.037 1.848 1.959 2.452 1.882 1.922 2.660 1.659	1.233 2.026 1.845 1.948 2.473 1.924 2.011 2.672 1.683	0.252 0.881 0.697 1.840 0.291 0.709 1.438 0.244 0.693	0.295 0.650 0.589 1.101 0.267 0.433 0.707 0.296 0.458	0.076 0.033 0.044 0.222 0.161 0.134 0.032 0.084 0.113	94 99 83 91 92 88 99 80	92 94 99 80 93 95 95 99 84	-23 12 -20 55 -74 6 53	-10 -8 -32 -31 -76 -31 -1 2 -61	-77 -95 -95 -86 -85 -79 -96 -65 -90	1.15E-7 1.72E-7 1.29E-7 5.77E-7 9.04E-8 1.60E-7 5.64E-7 1.56E-7 9.36E-8	3.13E-7 1.97E-6 3.41E-7 2.18E-6 1.80E-7 7.13E-7 4.77E-6 5.38E-6 2.36E-7	1.97E-5 1.50E-5 9.59E-6 1.10E-5 3.60E-7 1.23E-5 1.65E-5 2.96E-5 1.47E-6
Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT29 SW-620	0.450 0.764 0.315 0.356 0.281 0.245	1.414 2.390 2.183 2.124 1.224 1.862	1.456 2.485 2.151 2.036 1.238 1.744	1.416 2.429 1.838 1.783 1.319 1.847	0.265 0.134 0.186 0.243 0.176 0.399	0.200 0.067 0.176 0.248 0.116 0.197	0.105 0.039 0.027 0.022 0.088 0.098	104 106 98 95 101 93	100 102 82 81 110 99	-41 -82 -41 -32 -38 10	-56 -91 -44 -30 -59 -20	-77 -95 -92 -94 -69 -60	1.13E-7 9.60E-8 9.05E-8 9.37E-8 1.28E-7 1.77E-7	2.56E-7 1.79E-7 2.32E-7 2.60E-7 2.78E-7 1.06E-6	2.04E-6 3.34E-7 6.60E-6 1.02E-5 1.92E-6 2.83E-5
CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	0.589 0.799 1.079 0.772 0.954 0.346	2.011 2.721 2.832 2.502 1.673 1.248	1.931 2.656 2.800 2.410 1.444 1.209	1.932 2.744 2.747 2.363 1.397 1.187	0.841 0.565 1.183 1.623 1.270 0.258	0.691 0.333 0.638 1.084 0.671 0.074	0.068 0.004 0.088 0.107 -0.005 0.014	94 97 98 95 68 96	94 101 95 92 62 93	18 -29 6 49 44 -26	7 -58 -41 18 -30 -79	-88 -100 -92 -86 -100 -96	1.90E-7 1.23E-7 1.60E-7 4.79E-7 2.27E-7 1.16E-7	5.94E-6 2.98E-7 6.70E-7 7.45E-6 1.98E-6 3.05E-7	1.98E-5 2.58E-6 7.55E-6 2.25E-5 9.72E-6 1.44E-6
Melanoma LOX IMVI MALME-3M M14 MDA-MB-435 SK-MEL-2 SK-MEL-2 SK-MEL-2 SK-MEL-5 UACC-257 UACC-62	0.493 0.845 0.628 0.598 0.820 0.705 0.812 0.963 0.761	2.846 1.710 2.173 2.780 1.236 1.796 2.826 1.790 2.699	2.769 1.704 2.155 2.874 1.208 1.848 2.763 1.676 2.597	2.666 1.751 1.974 2.870 1.207 1.730 2.589 1.634 2.447	0.129 1.278 0.857 0.635 0.595 0.754 0.164 0.814 0.654	0.060 0.847 0.638 0.466 0.434 0.525 0.024 0.452 0.786	0.023 0.086 0.141 0.037 0.081 0.161 0.008 0.041 0.087	97 99 104 93 105 97 86 95	92 105 87 104 93 94 88 81 87	-74 50 15 2 -27 4 -80 -15 -14	-88 1 -22 -47 -26 -97 -53 1	-95 -90 -78 -94 -90 -77 -99 -96 -89	8.99E-8 5.00E-7 1.63E-7 1.14E-7 1.55E-7 8.44E-8 1.05E-7 1.16E-7	1.80E-7 5.02E-6 5.10E-6 5.88E-7 2.96E-7 7.05E-7 1.68E-7 3.46E-7	3.59E-7 1.80E-5 2.22E-5 1.22E-5 5.85E-6 1.49E-5 3.32E-7 4.14E-6 1.86E-5
Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 NCI/ADR-RES SK-OV-3	0.722 0.409 0.700 0.583 0.540 0.584 0.677	2.297 1.373 1.599 1.597 1.814 1.972 1.203	2.285 1.406 1.557 1.570 1.707 2.014 1.224	2.448 1.412 1.451 1.631 1.701 1.990 1.247	0.940 0.485 0.930 0.793 0.597 0.715 0.891	0.603 0.180 0.770 0.540 0.552 0.483 0.727	0.203 0.034 0.031 0.194 0.063 0.305 0.011	99 103 95 97 92 103 104	110 104 83 103 91 101 108	14 8 26 21 4 9 41	-17 -56 8 -7 1 -17 9	-72 -92 -96 -67 -88 -48 -98	2.09E-7 1.82E-7 1.89E-7 2.21E-7 1.49E-7 1.81E-7 3.64E-7	1.43E-6 6.64E-7 5.94E-6 2.73E-6 5.12E-6 1.13E-6 6.11E-6	2.01E-5 4.03E-6 1.81E-5 2.61E-5 1.86E-5 > 5.00E-5 1.78E-5
Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UO-31	0.761 1.358 0.480 0.655 0.996 0.940 0.937 0.913	2.288 2.609 1.719 2.982 1.889 3.119 1.487 2.320	2.354 2.429 1.714 2.876 1.812 3.021 1.416 2.128	2.357 2.439 1.687 3.186 1.773 2.962 1.599 2.267	0.754 1.663 0.177 0.456 0.529 1.287 0.832 0.143	0.199 0.336 0.154 0.742 0.190 0.873 0.606 0.041	0.057 0.034 0.106 0.006 0.083 0.167 0.016 0.038	104 86 100 95 91 96 87 86	105 86 97 109 87 93 120 96	24 -63 -30 -47 16 -11 -84	-74 -75 -68 4 -81 -7 -35 -96	-93 -97 -78 -99 -92 -82 -98 -96	1.64E-7 1.93E-7 9.87E-8 1.32E-7 9.44E-8 1.80E-7 1.71E-7 9.02E-8	4.89E-7 8.78E-7 2.02E-7 2.23E-7 2.44E-6 4.11E-7 1.71E-7	2.35E-6 2.79E-6 4.14E-7 1.67E-5 6.17E-7 1.86E-5 8.55E-6 3.23E-7
Prostate Cancer PC-3 DU-145	0.785 0.321	1.976 1.655	1.905 1.619	1.902 1.554	0.895 0.485	0.540 0.294	0.150 0.015	94 97	94 92	9 12	-31 -9	-81 -95	1.65E-7 1.69E-7	8.44E-7 1.94E-6	1.19E-5 1.50E-5
Breast Cancer MCF7 MDA-MB-231/ATC HS 578T BT-549 MDA-MB-468	0.510 C 0.664 1.143 1.144 1.213	2.644 1.718 2.579 2.229 2.380	2.428 1.682 2.534 2.264 2.315	1.822 1.756 2.403 2.191 2.199	0.834 0.856 1.805 1.112 1.261	0.556 0.772 1.425 1.001 0.473	0.224 0.096 0.942 0.021 0.205	90 97 97 103 94	61 104 88 96 84	15 18 46 -3 4	2 10 20 -13 -61	-56 -86 -18 -98 -83	8.84E-8 2.12E-7 4.03E-7 1.47E-7 1.34E-7	5.44E-6 6.39E-6 1.68E-5 4.68E-7 5.77E-7	3.92E-5 2.13E-5 > 5.00E-5 1.37E-5 3.38E-6

	EXPERIMENT: AAZ-884/0/	/ 8R	THMOR: NO CELLS	HOST: Athymic Nude		IMPLANT DATE: 11-ALG-2015
	MEMO NO: BOOK NO:		SOURCE/LINE: 0 IMPLANT SITE: 0	SOURCE: BTB SEX: F	H.	STAGING DATE: 11-AUG-2015 EVALUATION DATE: 25-AUG-2015
	TR	EATMENT				
Grp Nt	SC Dose/Units Rt.	. Schedule	Death Days	Surv/Total Day 14		
4 D-S7	82135 100.00 mg/kg/dose IP	QD X 1, Day 0	I	1/1		
5 D-S7	'82135 200.00 mg/kg/dose IP	QD X 1, Day 0	I	1/1		
6 D-S7	'82135 400.00 mg/kg/dose IP	QD X 1, Day 0	2	1/0		
VEHICLE	S					
Grp 4 ⇒	> NSC # S782135 / 2 (Dose =	= 100.00)	: in 100% DMSO	(Soluble - no visible particles)	200.0 mg/ml	Inj. Vol.: 0.5 ul/gm body wt
Grp 5	> NSC # S782135 / 2 (Dose =	= 200.00)	: in 100% DMSO	(Soluble - no visible particles)	200.0 mg/ml	Inj. Vol.: 1 ul/gm body wt
Grp 6 ⇒	 NSC # S782135 / 2 (Dose = 	= 400.00)	: in 100% DMSO	(Soluble - no visible particles)	200.0 mg/ml	Inj. Vol.: 2 ul/gm body wt

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			ody weight.	I treatment was administered according to exact l	NOTE: AI
Inj. Vol.: 2 ul/gm bo	200.0 mg/ml	(Soluble - no visible particles)	: in 100% DMSO	NSC # S782135 / 2 (Dose = 400.00)	Grp 6 ⇒
Inj. Vol.: 1 ul/gm bo	200.0 mg/ml	(Soluble - no visible particles)	: in 100% DMSO	NSC $\#$ S782135 / 2 (Dose = 200.00)	Grp 5 ->
Inj. Vol.: 0.5 ul/gm b	200.0 mg/ml	(Soluble - no visible particles)	: in 100% DMSO	NSC # S782135 / 2 (Dose = 100.00)	Grp 4 ->

IV. (b) ii) Nontumored Animal Toxicity Assay for Compound 11

(c) Cytotoxicity Data Against Cancer Cell Lines HEK 293T, MES SA, and MES SA DX

Material and Methods

Cytotoxity Assay.

Cells were cultured in a T75 flask to ~ 50–80 % confluency and harvested with trypsin into a single cell suspension. Five hundred (500) cells per well were seeded in tissue culture plates in 50 μ L/well culture media and incubated at 37 °C for 18–24 hours. Compounds were diluted as 400x final desired concentrations in DMSO. Serial dilutions in DMSO were then diluted in culture media for a final DMSO concentration of 0.25 % and 50 μ L/well of the final dilution was added to the cells (Vf = 100 μ L). Upon plating and treatment, cells were returned to the incubator for an additional 72 hours. CellTiter-Glo reagent was prepared per manufacturer's instructions and added at 100 μ L/well to the cultures. CellTiter-Glo allows for relative enumeration of metabolically active cells by quantifying intracellular ATP concentrations. After 5 minutes of incubation with CellTiter-Glo at room temperature, 125 μ L/well of the Cell Titer Glo/cell lysate solution was transferred into black assay plates, which were then read in a luminometer within 30 minutes. Luminescence readings obtained from cultures that did not receive any treatment (cell culture media only) were set as 100 % control and all other luminescence values were normalized to these controls (e.g., Normalized RLU, relative luminescence unit).

Cell lines used in the assay:

MES SA and MES SA/Dx cells are uterine sarcoma. MES SA Dx cell line was generated from MES SA to achieve upregulation of MDR1. MES-SA/Dx cells exhibit marked cross-resistance to a number of chemotherapeutic agents (including daunorubicin, dactinomycin, vincristine, taxol, colchicine) and moderate cross-resistance to mitomycin C and melphalan.

293T cells are human embryonic kidney cell line.

















V. ¹H-NMR and ¹³C-NMR Spectra of Compounds



¹³C-NMR (151 MHz, CDCl₃)


































































































































210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 fl (ppm)























































































































































































































































































¹H NMR (600 MHz, CDCl₃)











VI. References

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