Supplementary Figure 1: Determination of whether Doxo is deleteriously affected by (BDI)ZnN(TMS)$_2$ during the initiation steps.

(a) 

(b) 

(c) 

(d)
**Figure S1**  HPLC analysis of (a) Doxo treated with \((\text{BDI})\text{ZnN(TMS)}_2\) and (b) Doxo treated without \((\text{BDI})\text{ZnN(TMS)}_2\). ESI-MS analysis of Doxo treated (c) with \((\text{BDI})\text{ZnN(TMS)}_2\) and (d) without \((\text{BDI})\text{ZnN(TMS)}_2\).

**Experimental:** In a glove box, Doxo (5.8 mg, 0.01 mmol) was mixed with \((\text{BDI})\text{ZnN(TMS)}_2\) (6.4 mg, 1.0 equiv.) in 300 μL of THF. The mixture was stirred for 15 min at room temperature, and then 200 μL of methanol and 50 μL acetic acid were added to the mixture to dissociate the BDI-metal complex from Doxo. The solution was stirred at room temperature for an additional 30 min. All solvents were then evaporated under vacuum. The residue was reconstituted with a mixture of acetonitrile and methanol \((v/v = 1/1)\) and analyzed by HPLC (trace a). Doxo treated similarly but without \((\text{BDI})\text{ZnN(TMS)}_2\) was used as a control (trace b). These two Doxo samples, treated with and without \((\text{BDI})\text{ZnN(TMS)}_2\), were also analyzed by high resolution ESI-MS (trace c and d, respectively). High resolution ESI-MS results: For (c) Doxo treated with \((\text{BDI})\text{ZnN(TMS)}_2\), MS (HR-ESI): calcd. for \(\text{C}_{27}\text{H}_{30}\text{NO}_{11}\) [\(\text{M + H}\)]\(^+\) \(m/z\) 544.1819, found \(m/z\) 544.1832. For (d) the Doxo control (Doxo treated without \((\text{BDI})\text{ZnN(TMS)}_2\)), MS (HR-ESI): calcd. for \(\text{C}_{27}\text{H}_{30}\text{NO}_{11}\) [\(\text{M + H}\)]\(^+\) \(m/z\) 544.1819, found \(m/z\) 544.1829.
Supplementary Figure 2: Demonstration that Doxo is released in its original form from PLA-Doxo NC.

Figure S2. HPLC analysis of the authentic Doxo (red trace) and the Doxo released from Doxo-LA$_{10}$ after incubation in 1× PBS at 37°C for 10 days (black trace). The spectra were recorded on a System Gold 128 UV detector between 200 and 600 nm (Beckman Coulter, Fullerton, CA).
**Supplementary Figure 3** Succinic anhydride (SA), as the analogue of LA, was used to assess if the C14-hydroxyl group of Doxo preferentially initiates the LA polymerization in the presence of (BDI)ZnN(TMS)$_2$.

(a) 

![Chemical Structures](image)

(b) 

![NMR Spectra](image)

(c) Chemical Shift

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Figure S3. (a) Schematic illustration of the anticipated ring opening of succinic anhydride (SA) by the C14-OH of Doxo when SA was treated with Doxo/(BDI)ZnN(TMS)$_2$. (b) $^1$H NMR analysis (DMSO-$d_6$) of Doxo and Doxo-succinic ester (Doxo-SE) to confirm the attachment of SE to the C14-OH of Doxo and formation of Doxo-SE. (c) $^1$H NMR chemical shifts of Doxo and Doxo-SE. (d) HPLC analysis of (i) the reaction mixture of SA (1 equiv.) and Doxo/(BDI)ZnN(TMS)$_2$ (1/1.2 molar ratio) and (ii) Doxo-SE incubated in 1× PBS solution at 37°C for 48 h. (e) ESI-MS analysis of the compound derived from the reaction of SA with Doxo/(BDI)ZnN(TMS)$_2$ (i, Figure S3d).
Experimental procedures:

In a glove box, Doxo-HCl (2.0 mg, 0.0035 mmol) was mixed with (BDI)ZnN(TMS)$_2$ (2.4 mg, 1.2 equiv.) in THF (200 µL) for 30 min. The solvent was then evaporated. Freshly recrystallized SA in THF solution (0.41 mg, 1.2 equiv) was added dropwise to the mixture of (BDI)ZnN(TMS)$_2$ and Doxo and stirred for an additional 60 min. The reaction was monitored by HPLC. Separation and purification of Doxo-SE were conducted on a HPLC equipped with an analytical C18 column (Luna C18, 250 × 4.6 mm, 5 µ, Phenomenex, Torrance, CA). The fractions containing Doxo-SE were combined, lyophilized and dissolved in anhydrous DMSO-$d_6$ for NMR analysis on a U1500NB system. The high resolution ESI-MS analysis of Doxo-SE was performed on a Micromass Q-TOF Ultima system. MS (HR-ES): calcd. for C$_{31}$H$_{34}$NO$_{14}$ [M + H]$^+$ m/z 644.1979; found m/z 644.1987.
Supplementary Figure 4. HPLC was used to monitor Gos-initiated LA polymerization and release of Gos from Gos-PLA using NaOH.

Figure S4. HPLC analysis of the free Gos (trace i, black), the solution for the polymerization of LA (100 equiv.) mediated by Gos/(BDI)MgN(TMS)$_2$ (trace ii, red) and the solution of Gos-LA$_{100}$ treated with 0.1 NaOH (trace iii, blue). HPLC analysis clearly showed that Gos could be efficiently incorporated to PLA (ii) and released from Gos-LA$_{100}$ to its original form.