Remarks

Claims 1-18 are pending in the subject application. By this Amendment, Applicants have amended claims 1, 4, and 5. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-12 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

The application was filed with Figures 1-21. The Office Action Summary page did not indicate that the drawings were accepted or objected to by the Examiner. Applicants respectfully request that the Examiner consider the figures and indicate their status in the next communication.

Applicants appreciate permission of an Examiner Interview after final rejection to discuss the basis of the Applicants' position concerning the teachings of art cited in the Office Action.

Applicants respectfully submit that this amendment will require no further search or examination on the part of the Examiner and does not constitute new matter.

Claims 1-12 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants respectfully assert that the claims as filed are definite.

Claim 1 is amended to clearly define that the carbon is specifically the carbon substituted with the biologically active molecule of a repeating diene monomer unit of the polymer backbone and to clarify the separation between adjacent carbons of this type. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 1, 2, 4, 5 and 10-12 stand rejected under 35 U.S.C. § 103(a) as obvious over Valenti *et al.* (Macromolecules, 1998) and Elvira *et al.* (Molecule, 2005). Applicants respectfully assert that the claimed invention as amended is not obvious over the cited references.

As is appreciated by the Patent Office:

> *In re Hughes* holds that "***Words in a reference are to be construed in light of the relevant surrounding circumstances*** in each case, *In re Folkenroth*, 275 F.2d 732, 47 CCPA 812, and ***a reference in any event is good only for that which it clearly and definitely discloses. (emphasis added)***

The Office Action correctly indicates that Valenti *et al.* teaches the synthesis of well-defined polyalcohol homopolymers and suggests their use as "binding substrates in the preparation of a series of drug release macromolecules" (page 2773, col. 1, paragraph 1). Respectfully, the Examiner infers that the polyalcohols are not for directly binding drugs, but that they are taught for synthesis of a covalently bound drug. Applicants, which include a coauthor of Valenti *et al.*, hold that this statement did not suggest that binding is the use of the homopolymers therein as synthetic intermediates to prepare other homopolymers. There is no disclosure to transformation of the disclosed homopolymers with hydroxy groups to homopolymers with drug attachment to repeating units. Rather, Valenti *et al.*, uses drug binding of the traditional definition, that being "***Interacting selectively and non-covalently with a drug***" (European Bioinformatics Institute - Databases, http://www.ebi.ac.uk/QuickGO/GTerm?id =GO:0008144) (emphasis added)

Furthermore, Valenti *et al.* clearly states that "We intend ***to use these well-defined polyalcohol polymers as binding substrates*** in the preparation of drug release macromolecules." One skilled in the art would not look to a polyalcohol homopolymer for conversion of every hydroxyl group to a homopolymer having "a plurality of repeating diene monomer units, each of the repeating diene monomer units having coupled thereto at least one biologically active molecule", as in the instant claimed invention. It is well appreciated by those skilled in the art that very few organic homopolymers can be transformed by reaction of the side groups into a different homopolymer. The general view of those skilled in the art is that chemical transformation of side groups to form a second homopolymer from a first homopolymer is the exception and not the "obvious" rule. Arguably, the most used synthetic polymer textbook of all time is George Odian, *Principles of Polymerization*, wherein, as recited in the Third Edition, Chapter 9, pages 691 and 692, homopolymer preparation from another homopolymer is discouraged:

> "It is usually assumed that the reactivity of a functional group in a polymer and a small organic molecule are the same.... However, in many instances, the

> reaction rates and maximum conversion observed in the reactions of polymer functional groups differ significantly from those for the corresponding low-molecular weight homologues. ***Polymer reaction rates and conversions are usually lower,...*** *p. 691(emphasis added)*
>
> "***Yield or conversion in reactions of polymers means something quite different than in small molecule reactions when the conversion is less than 100%***. For example, 80% yield in the hydrolysis of methyl propanoate has no effect on the purity of the propraonic acid that can be obtained...The 80% yield simply limits the maximum amount of pure propanoic acid that can be obtained to 80% of theoretical yield. ***However, 80% yield in the corresponding hydrolysis of poly(methyl acrylate) does not result in 80% yield of polyy(acrylic acid) with 20% unreacted poly(methyl acrylate***). ***The product contains copolymer molecules***, each of which, on the average, contain 80% acrylic acid repeating units and 20% methyl acrylate units randomly placed alone the polymer chain. ***Unlike the corresponding small molecule reaction, the unreacted ester groups cannot be separated from the product since both are part of the same molecule***." *p. 692 (emphasis added)*

This teaching of Odian, though perhaps more clearly stated, is consistent with that taught in other common polymer textbooks. For example, Harry R. Allcock and Fredric W. Lampe, *Contemporary Polymer Chemistry*, Second Edition, pages 149-50 recites:

> In theory, the vast arsenal of conventional organic and inorganic reaction chemistry could be used to modify the side groups in a polymer. In practice, limitations exist. ***Reactions that proceed rapidly and efficiently at the small-molecule level may not take place effectively with a high polymer***" *p. 149-50 (emphasis added)*
>
> "***There exists one polymer system*** -the polyphosphazines- ***in which macromolecular substitution reactions are so efficient that such reactions are the main method of polymer synthesis and structural diversity....Unfortunately, such intermediates are all too rare among organic polymer systems***. *p. 150 (emphasis added)*

Clearly, even if the Valenti *et al.* statement of "binding substrates in the preparation of a series of drug release macromolecules" (page 2773, col. 1, paragraph 1) would encourage their chemical modification to form a macromolecule with bonded drugs, one of ordinary skill in the art would appreciate that a copolymer is suggested and not a homopolymer "consisting of a plurality of repeating diene monomer units, each of the repeating diene monomer units having coupled thereto at least one biologically active molecule," of amended claim 1. Clearly, in more than 17 years since the submission of the preliminary manuscript that led to Valenti *et al.* on October 8, 1997, no disclosure of a homopolymer with bioactive agents on every repeating unit

from the well-defined polyalcohol polymers of Valenti *et al.* has resulted from that research group or any other.

Elvira *et al.* teaches drug delivery systems containing a polymeric backbone conjugated at pendant groups to a bioactive molecule. Elvira *et al.* teaches a variety of hydrolyzable or biodegradable linkers: esters; carbonates; anhydrides; urethanes; orthoesters; and amides that have been used to make polymer-drug conjugates. Elvira *et al.* does not teach a single polymeric system where the pendant drugs are at a regular interval along the backbone of a homopolymer chain or a polymeric chain prepared by step-growth polymerization. Elvira *et al.* only teaches the preparation of copolymers, where bioactive agents are on one or more repeating units of a polymer prepared by a chain-growth polymerization, and does not suggest the preparation of a homopolymer. Elvira *et al.* teaches pendent group systems, where it clearly states in the introduction, page 119, where these pendent group systems are directed exclusively to copolymers. All pendent systems disclosed therein are copolymers.

Therefore, those of ordinary skill in the art, as evident the teaching of Odian in *Principles of Polymerization*, would not be motivated to carry out a polymer modification of the polyalcohol polymer of Valenti *et al.*, to yield a homopolymer with biologically active molecules attached to every repeating unit. Elvira *et al.* reinforces Applicants' view that the polymer modification indicated in the Office Action would not be considered a viable synthesis of a homopolymer such as that of the instant invention, as Elvira *et al.* exclusively teaches copolymers, including copolymers prepared by polymer modification that does not proceed to a homopolymer. Hence, the homopolymers of the amended claimed invention cannot be obvious in view of the copolymers taught in Elvira *et al.* and the binding substrate suggested in Valenti *et al.*

Claims 3 and 6-9 stand rejected under 35 U.S.C. § 103(a) as obvious over the combination of Valenti *et al.* (Macromolecules, 1998) and Elvira *et al.* (Molecule, 2005), as applied to claims 1-2, 4-5, 10-12, above and further in view of Zhu (Acc. Chem Res., 2002). Applicants respectfully assert that the claimed invention is not obvious over the cited reference.

The Office Action indicates that the combination of Valenti *et al.* and Elvira *et al.* fail to teach a linker that comprises an ether group and a carbamate group. The combination of Valenti *et al.* and Elvira *et al.* also fail to teach an ethylene glycol or multiple ethylene glycol spacers.

As indicated above Valenti *et al.* in view of Elvira *et al.* does not obviate the instant claimed invention, as a homopolymer is neither taught nor suggested by the combination. Zhu does not cure the deficiency of Valenti *et al.* in view of Elvira *et al.* There is not a single polymer taught in Valenti *et al.*, Elvira *et al.*, or Zhu that is a regular step-growth polymer with pendant biologically active groups. All polymers with pendant biologically active groups are copolymers. The present application discloses new compositions of matter that are homopolymers and these homopolymers are neither taught nor suggested by Valenti *et al.* in view of Elvira *et al.* further in view of Zhu. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

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